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IN THIS ISSUE

Interest in the health of the population of Paris under the German occupation naturally is great, but little definite information has been available. Mortality statistics and other data relating to approximately the first year of occupation were assembled by Dr. Ramon F. Minoli, who left Paris in November, 1941, and are presented in the article "Food Rationing and Mortality in Paris, 1940-1941." A striking increase in tuberculosis occurred in this first year of food restrictions, and the new cases were characterized by rapid development and high fatality. Food rations were relatively least deficient for young children and most inadequate for old persons, and mortality among the latter group was very high. Since the effects of continued diet deficiencies are most certainly progressive, health conditions and mortality in Paris no doubt have become much worse.

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Morbidity surveys have shown that females are ill more frequently than are males. Since at any specific age period mortality is higher for males than for females, additional study of sex differences in morbidity is of interest. The article "The Severity of Illness Among Males and Females," by Sally Preas of the Fund's staff and Ruth Phillips of the United States Public Health Service, presents a further investigation of sex differences in morbidity. Severity of illness was tested according to (1) degree of disability, (2) duration of disability, and (3) the amount of medical care for illness. The results indicate that even though the rate of illness was greater for females, on the whole the illnesses reported for males were considerably more severe than those reported for females.

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Between the widespread prevalence of dietary inadequacies revealed by surveys and the relatively infrequent occurrence of deficiency diseases reported by clinicians has existed a seeming contradiction. In an article entitled "A Concept of the Deficiency States," Dr. H. D. Kruse points out that the recorded prevalence of malnutrition depends on the concept of deficiency diseases and the methods of recognizing them.

Reports on the infrequency of deficiency diseases have tacitly referred solely to the classic frank type. Of these, the prevalence is low. But most of the defi-

ciency diseases are not of this type. In reality, deficiency states are widely prevalent. Recognition of their characteristics and application of new methodology are necessary for their detection.

Based on observations of tissue changes in four deficiency diseases, Dr. Kruse outlines the various states in which these disorders actually occur in the population. He points out that almost all the literature on deficiency diseases, all clinical examinations of persons and experiments with animals, have dealt with the severe acute forms; whereas in this country the most prevalent states are mild or severe chronic with or without a mild acute process superimposed. The reasons for the high prevalence of these states are also explained.

Dr. Kruse calls attention to the importance of time in the course of deficiency diseases, particularly chronic forms, in which several changes previously attributed to the aging process are shown to be manifestations of deficiency states. These changes have now been demonstrated to be reversible. He emphasizes that recession of the chronic processes under therapy occurs at a slow rate and requires a long period for completion.

The concept also explains the restricted application of blood and urine methods in the appraisal of nutritional status and the circumstances under which they may be misleading.

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In the medical evaluation of nutritional status, methods have been needed for detecting all states of avitaminosis C and aniacinosis. In two papers Dr. H. D. Kruse reports on "The Lingual Manifestations of Aniacinosis" and "The Gingival Manifestations of Avitaminosis C," with especial consideration in both to the detection of early and mild changes by biomicroscopy.

Presenting observations on the changes in the tongue and gums, early sites of involvement in aniacinosis and avitaminosis C, respectively, the papers describe the lesions in various stages of development, from very early to far-advanced. Gross and biomicroscopic examination of the tongue and gums for these characteristic changes permits detection of aniacinosis and avitaminosis C in any states. Just as the biomicroscope proved indispensable in permitting detection of the initial and mild conjunctival and corneal changes in avitaminosis A and ariboflavinosis, it is shown to be invaluable again in revealing subclinical lingual and gingival alterations in aniacinosis and avitaminosis C.

These two new methods, together with those previously reported for avitaminosis A and ariboflavinosis, form a battery of simple, convenient, and objective procedures for the appraisal of nutritional status.

It is also shown that recession of the chronic process, in aniacinosis and avitaminosis C as in ariboflavinosis and avitaminosis A, under potent, specific therapy is complete only after a prolonged period.

FOOD RATIONING AND MORTALITY IN PARIS, 1940-1941

RAMON F. MINOLI, M.D.[1]

FOOD rationing started throughout France on October 1, 1940, and a card system was evolved by age, occupation, and state of health. The following foods were restricted: bread, meat, cheese, fats (lard, oil, etc.), sugar, milk, chocolate, and milled products. Technically other foods could be obtained, but in reality it was difficult to get them; horsemeat, fish, and fowl were very scarce. At first potatoes were sold without restriction, but they were rationed later. They were issued in quantities varying from two to six pounds per person. Different kinds of tubers of slight nutritive value were sold to the public; such as turnips and rutabagas, which had formerly been used to feed cattle. All fruits became scarce; and prices doubled creating very serious difficulties for the lower income classes. It should be noted, too, that it was not possible to procure the full ration of meat allowed on each card. In reality, only ninety grams of meat per week was obtainable. However, that part of the population having relatives or friends in the country, received foods from them. There existed, furthermore, in the big cities, "Black Markets," where certain foods could be purchased, but these only by a few for the prices were outrageously high.

Table 1 gives the protein, fat, carbohydrate, and caloric value of foods rationed according to age, occupation, and state of health, as devised for France.

Four special basic diets were likewise devised for sick persons in the following categories: those with diseases accompanied by fever, where a milk diet alone was prescribed, were allowed 1,158 calories; cardiacs, nephritics, etc., on lacto-vegetarian diets, were allotted

[1] Dr. Minoli, now in the United States, returned from Paris in November, 1941, after spending three years in France. Dr. Minoli is in the Medical Service, Department of Immigration, Republic of Argentina, and is Assistant Director of Service of Professor Tobias, Director of Public Assistance, Buenos Aires.

Classifications	Protein (Grams)	Fat (Grams)	Carbohydrates (Grams)	Total Calories
1 to 3 Years	42.86	48.94	125.80	1,151
3 to 6 Years	50.81	51.04	168.53	1,379
6 to 13 Years	37.99	35.57	180.05	1,228
13 to 21 Years	34.95	29.62	211.87	1,290
21 to 70 Years	28.91	25.27	163.18	1,025
70 Years and Up	25.31	25.54	133.28	890
Workmen and Farm Laborers	33.79	26.02	201.23	1,208
Workers (Light Industrial)	36.87	35.04	201.24	1,305
Workers (Heavy Industrial)	39.95	44.06	201.31	1,403

Table 1. Food value per day of rations in France, 1940-1941.

1,164 calories; diabetics on carbohydrate-restricted diets, 1,489 calories; nephritics on a meat-restricted diet, 1,542 calories.

Average Total Diet in Paris

Because some food could be procured in addition to the basic ration, it is difficult to obtain a true idea of what the persons living in Paris really consumed. In a series of reports made to scientific societies throughout France, estimates have been based on the rations indicated on the cards, without taking into consideration the undetermined portions that each individual could have secured from other sources. This has been conducive to estimating exaggerated quantitative and qualitative insufficiencies.

A survey by H. Gounelle and R. Mande, of the Institut des Récherches d'Hygiene gives data on how different families of Paris were feeding themselves. Specially trained nurses made a thorough study in sixty-five different homes, and each day for one week, they weighed all the food consumed by members of the family of both sexes whose ages were between 20 and 50 years. The survey was carried out in May, June, and July, 1941. The results of this study more nearly approximate the actual situation. Table 2 shows the average daily consumption per person.

From this survey, Gounelle and Mande conclude that the diets studied show:

1. A total caloric insufficiency of about a thousand calories daily.
2. A calcium deficiency and a calcium-phosphorus imbalance.
3. An insufficient amount of Vitamin A.

Tuberculosis in Paris. It is undoubtedly a fact that morbidity and mortality caused by tuberculosis have noticeably increased in Paris. The percentage of rapidly-developed tuberculosis has gone up in an alarming manner. To illustrate this we have taken some figures from a report presented in September, 1941, to the Academie de Medecine de Paris by Dr. Marcel Moine, Chief of Statistics of the Comité National de Defense Contre La Tuberculose.

Comparing the figures of the first six months of 1941 with the corresponding ones in 1939, we find that the mortality of tuberculosis increased 10 per cent. In children under one year of age, the increase was 15 per cent. In children from one to nine years, the increase was 28 per cent. The deaths from pulmonary tuberculosis increased 20.4 per cent, and from other types of tuberculosis increased 30.4 per cent.

Table 2. Average daily food consumption by adult persons in Paris estimated by Gounelle and Mande from a study of sixty-five families.

Nutrient	Quantity	Calories	Calories (Per Cent of Total)
Protein	69.46 gms.	277.84	15.9
Fat	38.00 gms.	342.00	19.6
Carbohydrate	281.70 gms.	1,126.80	64.5
		1,794.64	100.0
Calcium	0.438 gms.		
Phosphorus	1.118 gms.		
Iron	0.016 gms.		
Vitamin[1] A	3,472 I.U.		
Vitamin[1] B_1	340. I.U.		
Vitamin[1] C	65. milligrams		
Vitamin[1] D	0.71 I.U.		

[1] Vitamin estimates based on diets of only thirty persons.

In reference to morbidity, Moine, comparing the volume of work done in the laboratory department of l'Oise in the first semester of 1938 with that done in the corresponding semester of 1941, gives the following figures:

The requests for sputum examinations increased 38 per cent in the Beauvais Dispensary, and 101 per cent in Compiègne.

The positive results found in the sputum examinations of those coming to the dispensaries for the first time, showed an increase of 44.5 per cent in Beauvais and 47.3 per cent in Compiègne.

In five dispensaries an ominous increase was observed in the proportion of positive bacillus sputums per thousand sputum examinations. The average figures from five laboratories were as follows:

1938— 54.3	positive	results	per	thousand	sputum	examinations.
1939— 59.1	"	"	"	"	"	"
1940— 72.2	"	"	"	"	"	"
1941—211.0	"	"	"	"	"	"

Thus, in the first half of 1941, there was an increase of 270 per cent as compared with the average figures for 1938 and 1939.

The department covering social insurance has also determined an increase in tuberculosis morbidity among the insured. Those reacting to the tuberculin tests were not only more numerous but they were also younger.

Ravina, Pecher, Bucquoy, and C. Pujol[3] point out the importance and gravity of forms of pulmonary tuberculosis which are actually seen and they indicate as possible causes: the summoning to the army or Civil Service of old tuberculosis patients considered as cured, or of young people who have not been thoroughly examined; moral factors (evacuation, separation from a familiar environment, etc.), and malnourishment.

In the discussion of this report, Rist also pointed out that an in-

[3] *Bulletin de la Societé Médicale des Hôpitaux de Paris*, Nos. 17 and 18, July, 1941, pp. 464-469.

crease has actually been observed in the proportion of cases of rapidly fatal tuberculosis.[8] Ameuille indicated that a characteristic of present-day tuberculosis is the increase of caseous pneumonia. Only two or three cases a week of pneumonia tuberculosis formerly were seen in his department; now there are from five to ten. Brule has also observed the increase in serous tuberculosis; the rapid development and early bilateralization of pulmonary tuberculosis make the use of pneumothorax more difficult. Etienne Bernard also pointed out the frequency of cervical tubercular adenopathies associated with evolutive pulmonary bacilli.

To lessen the ill effects upon persons with active tuberculosis and known lesions, a diet was given which corresponded to their general category, plus a supplementary amount of 45 grams of meat and 15 grams of fat daily per patient.

Despite the precaution indicated, the march of tuberculosis up to October, 1941, has been ominously progressive; thus, if the present dietary regime continues and the consequences increase, the problem of tuberculosis in France will be exceedingly grave.

General Mortality During the First Eleven Months of Food Rationing

The food restrictions to which the population of Paris were subjected from the first of October, 1940; the intense cold aggravated by a prolonged and rigorous winter; and the absolute lack of heating facilities due to the fact that only 50 kilos of coal were available per year for each family created special conditions which were in some measure responsible for an increased mortality in Paris.

A comparative study of the deaths in this period with a corresponding period for the previous years was made. We have divided the mortality according to the ages of the deceased and have compiled statistics from 0 to 1 year, from 1 to 9 years, from 10 to 19 years, from 20 to 59 years, and from 60 years upward. All the fig-

[8] Rist-Ameuille-Brule-Bernard: Discussion of the report of Ravina, *et al.*, footnote 2.

Age	Oct. 1936–Aug. 1937	Oct. 1937–Aug. 1938	Oct. 1938–Aug. 1939	Oct. 1939–Aug. 1940	Oct. 1940–Aug. 1941
0– 1	2,085	1,764	1,937	1,476	1,672
1–10	1,189	892	926	589	791
10–19	544	616	593	546	535
20–59	13,338	12,966	12,670	11,408	12,086

Table 3. Number of deaths occurring in eleven months for each of the years from 1936 to 1941. By age groups for persons up to 59 years of age.

ures are based on data supplied by the *Bulletin Bi-Mensuel de Statistique Municipal* of the City of Paris.

The number of deaths in Paris for the period of October 1, 1940, to August 31, 1941, was 33,346. The average number for the corresponding eleven months of the preceding four years was 31,015. Thus, there was an increase of 7.5 per cent. However, the increase in mortality during the months of restrictions was greater than these figures indicate because the population of Paris has decreased.[4]

The deaths for specific age groups occurring in five eleven-month periods are given in Tables 3 and 4. From these data, the following comments can be made:

1. Comparing the mortality of persons 60 years and over from October, 1940 through August, 1941, we find that the total number of deaths were 18,262, and for the same periods in each of the four preceding years the average was 15,130. This is an increase of 3,132 deaths, or 21 per cent.

2. The increase in mortality was especially noticeable in the winter months.

3. The number of deaths of children, adolescents, and adults under 60 years of age did not increase.

The most striking thing is the extraordinary increase in the mortality of the old people in December, 1940, and January, 1941. To

[4] The lack of accurate population estimates for Paris makes comparisons of mortality in the most recent period with previous years inexact. According to the census of 1936, Paris had a population of 2,830,000. On the basis of the number of ration cards distributed, it has been estimated that the population has decreased approximately 400,000 persons.

Month	Oct. 1936–Aug. 1937	Oct. 1937–Aug. 1938	Oct. 1938–Aug. 1939	Oct. 1939–Aug. 1940	Oct. 1940–Aug. 1941
Total	15,415	15,304	15,339	14,462	18,262
October	1,479	1,433	1,194	892	1,487
November	1,370	1,407	1,341	912	1,594
December	1,625	1,668	1,644	1,170	2,150
January	1,659	1,821	1,757	1,802	2,896
February	1,754	1,568	1,555	1,691	1,755
March	1,781	1,548	1,771	1,877	1,649
April	1,375	1,371	1,401	1,470	1,561
May	1,305	1,298	1,426	1,389	1,521
June	1,168	1,063	1,147	1,204	1,426
July	954	1,117	1,115	1,099	1,189
August	945	1,010	988	956	1,034

Table 4. Number of deaths by month occurring in eleven months for each of the years from 1936 to 1941. For persons 60 years of age and over.

explain this, one must take into account the lessening of vitality in old people, which makes it difficult for them to struggle against the adverse circumstances of their environment. Furthermore, the children, adolescents, and younger adults had rations which varied between 1,025 and 1,379 calories; the old people had rations of 890 calories.

The motive of the Public Authorities in making the restrictions more rigorous in the case of old people was the fact that these, due to their diminishing activity and the absence of vitality and growth, have fewer necessities than adults. They were indubitably sacrificed in order to better as far as possible, the ration for the adults and children who represent the productive force and the future of the community.

Specific Diseases. Gout, which in normal times was relatively frequent in France, if compared with that observed in the countries of southern Europe and in America, has recently disappeared. Before the war, in the out-patient ward of Professor Costes, of the Hôpital Cochin, of a series of patients treated, not a single one remains which has not been cured spontaneously.

The obese, with the exception of those with glandular distur-

bances, have profited extraordinarily by the present diet. All have reduced in weight; some more than 50 kilos.

Diabetes treatment encounters serious difficulties through the lack of insulin and the food rationing. Insulin is very scarce and even in the diabetic wards it is reserved only for the patients in the most serious condition. If, up to now, the mortality rate of diabetes has not increased, it is sure to do so if the present conditions are maintained through the coming winter, especially if insulin continues to be so scarce.

Avitaminosis. The anticipated changes, due to the lack of foods rich in vitamins, did not become apparent. According to R. Mande, the vitamin content of the rations assigned was sufficient, with the exception of vitamin A. In the hospitals of Paris there has been no greater frequency of rickets, scurvy, xeropthalmia, beri-beri, polineuritis, etc., than before. During some months, the schools administered vitamins in the form of candy.

THE SEVERITY OF ILLNESS AMONG MALES AND FEMALES[1]

SALLY PREAS AND RUTH PHILLIPS

VARIOUS surveys have shown that the average incidence of illness is higher among females than among males. In the Hagerstown study, Sydenstricker[2] found that males had an illness rate from all causes of 970 per 1,000 and that females had a rate from all causes, exclusive of puerperal conditions, of 1,215 per 1,000 per year. Rates of 720 per 1,000 males and 833 per 1,000 females for all causes except female genital and puerperal diseases, were reported by Collins[3] in a study of illness made by the Committee on the Costs of Medical Care and the United States Public Health Service among 9,000 families in eighteen states. Although there were some differences in the methods used in these studies and also differences in the level of illness observed, the female illness rate was found consistently to be higher than the male rate. Collins pointed out that the females had a higher rate than the males for bed illness as well as for total illness, and he raised the question as to "whether this indicates more frequent illness among females, a greater severity of illness, or better care of the illness that occurs."[4] In another report on the frequency and volume of doctors' calls in the same group of families, Collins[5] furnished additional information on this subject. He found that although females had more doctors' calls per

[1] From the Division of Public Health Methods of the National Institute of Health and the Milbank Memorial Fund.

[2] Sydenstricker, Edgar: The Illness Rate Among Males and Females. *Public Health Reports*, United States Public Health Service, July 29, 1927, 42, No. 30, pp. 1939-1957.

[3] Collins, Selwyn D.: Cases and Days of Illness Among Males and Females With Special Reference to Confinement to Bed. *Public Health Reports*, United States Public Health Service, January 12, 1940, 55, No. 2, pp. 47-93.

[4] *Op. cit.*

[5] Collins, Selwyn D.: Frequency and Volume of Doctors' Calls Among Males and Females in 9,000 Families Based on Nation-Wide Periodic Canvasses, 1928-31. *Public Health Reports*, United States Public Health Service, November 1, 1940, 55, No. 44, pp. 1977-2020.

1,000 population than males, the higher rate of calls for females was a reflection of the higher incidence of illness. Very little difference was noted between calls per attended case for each sex. Apparently, females did not have a greater amount of medical care in relation to illness than males.

In view of the findings reported above, it is of interest to analyze in some detail the data from a special study of morbidity now being conducted among a sample of white families in the Eastern Health District of Baltimore. This paper presents a further study of some of the implications of the sex difference in morbidity with special reference to severity of illness. Is the sex difference in incidence of illness among males and females accompanied by a difference in severity of illness? An excellent opportunity to study this question is presented in the records of illness collected from a relatively small population such as that which is being surveyed in the Eastern Health District of Baltimore.

When the special study was initiated, the Eastern Health District of Baltimore consisted of two city wards containing 11,896 white families or households, including 43,377 persons, and 3,413 colored households, including 13,784 persons.* As far as the white population is concerned, the district is considered fairly representative of the localities in the City in which the wage-earning population lives; that is, it contains some families in relatively poor economic circumstances, wage-earning families in moderate circumstances, relatively few families in the professional class, and no families that can be classed as wealthy. Consequently, the district cannot be considered as representative of Baltimore as a whole, but it is probably representative of the population which forms the majority in the City.

There are three hospitals within the Eastern Health District and

*A few months after the special study of illness was started, the Eastern Health District was enlarged so that it now includes a population of approximately 100,000. Any reference to the Eastern Health District in this paper, however, is to the former district composed of Wards 6 and 7.

two adjacent to it. Each of these hospitals has an outpatient department. Approximately 150 private physicians practice regularly within the district. However, during the first and second years' study, from 300 to 400 different private physicians served the observed population.

Data and Method of Study

The method of sampling in this particular study has been described in detail in a previous report.[7] It is sufficient here to say that the white families living in thirty-five city blocks scattered throughout the two wards formed the sample population. The plan of the study was to follow families that live in a group of houses in certain blocks rather than to follow a selected group of families. No attempt was made to continue visiting families that moved out of these houses during the period of the study, but the new families that moved into the houses vacated in the sample blocks were included in the study. Monthly visiting was employed in this study in order to secure accuracy in the reporting of illness. The record of illness started with the first visit to the family; no attempt was made to secure a report of illnesses which had occurred during a period preceding the first visit except illness existing on the day of the visit.

In the studies of illness conducted by periodic canvasses of families, "illness" may be considered to include any affection or disturbance of health which persists for a considerable part of one or more days. In this study, as in other family surveys, no specific definition of illness was formulated. The records of "illness" are of sicknesses reported by the household informant (usually the housewife), either as experienced by herself or as she observed them in her family.[8] Physical defects or deformities, even though disabling, were excluded from this analysis.

[7] Downes, Jean and Collins, Selwyn D.: A Study of Illness Among Families in the Eastern Health District of Baltimore. The Milbank Memorial Fund *Quarterly*, January, 1940, xviii, No. 1, pp. 5-26.

[8] The causes of illness as reported by the family informants were submitted to the

(Continued on page 224)

Studies of illness conducted by periodic canvasses of families afford two expressions of morbidity rates, namely, prevalence and incidence. By prevalence is meant the ratio of persons ill at a given time to the total persons in the population at that time. Incidence of illness expresses the rate of occurrence of illness in a population observed over a period of time. Since prevalence of illness is composed chiefly of cases of chronic illness and incidence is greatly weighted by acute (short duration) illnesses, data of prevalence and incidence are discussed separately. The section based on prevalence data will deal largely with observations secured by following chronic conditions present among members of 1,757 white families at the time of the first visit. The section based on incidence will deal with observations made on illnesses arising in the population during the twelve-month period ending June, 1940. No family observed less than two months has been included.

Severity of illness, both chronic and acute illnesses, may be described in various ways: (1) according to degree of disability; (2) if disabling, the duration of disability; and (3) the amount of medical care. It is of interest to examine sex differences with respect to these categories.

It has been shown in a previous report[9] that the sample population in the morbidity study was found to be representative of the white population of the district from which it was drawn with respect to age and size of household.

In this report the analysis has been based on illnesses for all ages. The age distribution of the population for males and females is shown in Table 1. It is evident that no important differences existed between the age composition of the male population and that of the female. Consequently, it has not been considered necessary to make

attending physician for confirmation or correction. The causes of illness for clinic attendance and hospital admission were checked against the records of the clinic or hospital where the service was given.

[9] Downes, Jean: Illness in the Chronic Disease Family. *American Journal of Public Health*, June, 1942, 32, No. 6, pp. 589-600.

Age Groups	Years of Life			
	Male	Female	Male	Female
	Per Cent		Number	
All Ages	100.0	100.0	2,713	2,770
0- 4	7.4	7.2	199	200
5-19	26.0	24.9	705	687
20-39	34.4	34.3	932	948
40-59	24.4	24.5	659	677
60+	7.8	9.1	211	251
Unknown Age			7	7

Table 1. Sex and age distribution of sample population observed during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.

any adjustment for differences in age in making comparisons between rates for males and females.

Prevalence of Illness

In this study, prevalence indicates the number of persons for whom an illness was reported on the first visit to the family during the year ending June, 1940.

Table 2 shows the prevalence of illness for each sex, classified

Table 2. Prevalence of illness, by sex, in the Eastern Health District of Baltimore, 1939-1940.[1]

Classification of Illness	Ratio per 1,000		Ratio of Prevalence for Females to That for Males
	Males (3,314)	Females (3,336)	
Total Cases	142.7	231.7	1.62
Acute Illness	44.3	69.8	1.58
Chronic Illness[2]	98.4	161.9	1.65
Major Chronic	52.5	92.3	1.76
Minor Chronic	45.9	69.6	1.52
Institutional Illness	0.4	0.3	0.75

[1] Prevalence of illness as of the first visit to the family, 1939–1940. The population includes 1,757 white families observed two months or longer.

[2] Illnesses included in the classes, "major" and "minor," are enumerated on page 226 of the text.

according to acute and chronic and institutional illness. Chronic illnesses are subdivided into those which are here termed as "major" and as "minor" illnesses. The group designated as "major" includes: *Mental Disease* or *Mental Deficiency, Neurasthenia* or *Nervous Breakdown, Heart Disease, Hypertension* or *High Blood Pressure, Arthritis, Diabetes, Varicose Veins, Gall-Bladder Disease, Ulcer of the Stomach or Duodenum, Chronic Nephritis, Cancer, Rheumatic Disease, Tuberculosis, Syphilis, Anemia,* and chronic illness as a result of *Accidents.* "Minor" chronic illness, the second group, includes: *Neuralgia, Neuritis, Lumbago, Hemorrhoids, Hernia, Chronic Indigestion, Chronic Cold and Cough, Chronic Bronchitis, Sinusitis, Asthma,* chronic *Skin Conditions, Backache,* and other ill-defined complaints which were reported as chronic conditions.

Other studies have shown that chronic illness constitutes the majority of illnesses prevailing in the population at a given time. In this study approximately 70 per cent of the illnesses reported on the first visit to the family were chronic conditions or complaints. This proportion was true of both males and females. However, the rate of prevalence was considerably higher for females than for males, with

Table 3. Distribution of cases of chronic illness[1] by degree of disability and by sex in the Eastern Health District of Baltimore, 1939-1940.[2]

Classification of Illness	Per Cent		Number of Cases	
	Male	Female	Male	Female
Cases of Major Chronic Illness[3]	100.0	100.0	174	308
Nondisabling	61.0	69.2	106	213
Disabling but not Confined to Bed	24.1	18.5	42	57
Confined to Bed	14.9	12.3	26	38
Cases of Minor Chronic Illness[3]	100.0	100.0	152	232
Nondisabling	85.6	89.2	130	207
Disabling but not Confined to Bed	11.8	4.3	18	10
Confined to Bed	2.6	6.5	4	15

[1] Chronic illness present at the first visit to the family.
[2] The population includes 1,757 white families observed two months or longer.
[3] Illnesses included in the classes, "major" and "minor," are enumerated above in the text.

excesses of 52 to 76 per cent in the various classes of illness. Institutional illness, which included a small number of cases, was less frequent among females than among males.

Disability. Cases were grouped according to the following classifications: nondisabling; disabling at some time during observation, but not confined to bed; cases confined to bed for one or more days. A disabling illness was defined as one which caused loss of one or more days from work, school, or other usual activities during the period of observation.

The distribution of "major" and "minor" chronic illnesses by degree of disability is shown for each sex in Table 3. In the group of "major" chronic illnesses the proportion of cases which had some disability was higher among males than among females. This was true for both degrees of disability, (1) confined to bed and (2) disabling but not confined to bed. The same relationship between the sexes was noted for "minor" chronic illnesses, with one exception: the proportion classed as confined to bed was higher for females than for males. These differences between the sexes may be due in part to more complete reporting of nondisabling chronic conditions for females than for males, rather than to any true sex difference in disabling illness.

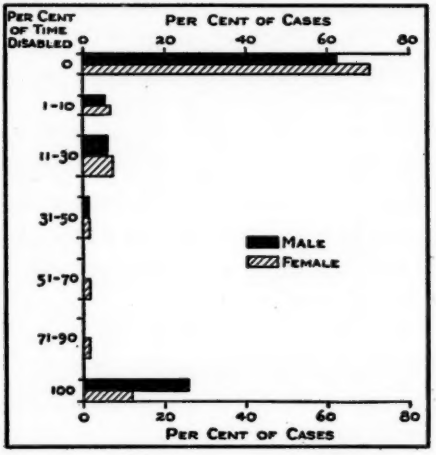

Fig. 1. Distribution of cases of "major" chronic illnesses according to the percentage of total days (duration of the case) that were disabled days.

Duration of disability for chronic illnesses may be expressed as a

frequency distribution of cases showing the proportion of the total time observed that the case was disabled because of the chronic illness itself. Figure 1 presents the data for "major" chronic illnesses for each sex. It is apparent that a large proportion of these illnesses caused no disability during the period of observation; 63 per cent of male cases and 70 per cent of female cases were in this class. There is a marked difference between the sexes when cases disabled throughout the period of observation are considered. Only 12 per cent of the female cases reported disability of such duration compared with 26 per cent of the male cases. Even though female cases which were disabled more than half of the time observed be added to this group, an excess of 50 per cent still remains in the number of male cases over female cases which were so severely disabled.

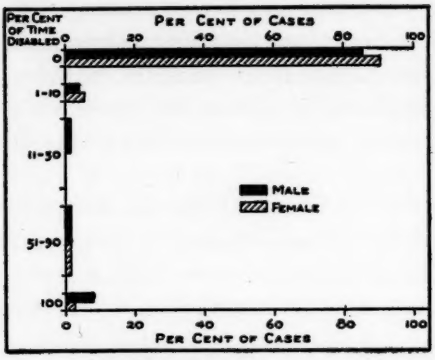

Fig. 2. Distribution of cases of "minor" chronic illnesses according to the percentage of total days (duration of the case) that were disabled days.

The chronic illnesses classed as "minor" caused less disability than did other chronic cases. Data for these "minor" cases are presented in Figure 2. In 86 per cent of the male cases and 91 per cent of the female cases the chronic condition caused no disability. Again the proportion of cases disabled throughout the period of observation was greater for males than for females.

Medical Care. Another index of severity is medical care in relation to illness. Table 4 shows the proportion of chronic illnesses which received medical care, private physician or clinic care. There was relatively little difference between the sexes; when "major"

Classification of Illness	Male	Female
Cases of Major Chronic Illness[2]		
Total Cases	174	308
Number Receiving Medical Care	86	138
Per Cent Receiving Medical Care	49.4	44.8
Cases of Minor Chronic Illness[2]		
Total Cases	152	232
Number Receiving Medical Care	37	66
Per Cent Receiving Medical Care	24.3	28.4

[1] The population includes 1,757 white families observed two months or longer.
[2] Illnesses included in the classes, "major" and "minor," are enumerated on page 226 of the text.

Table 4. Per cent of chronic illnesses which received medical care at some time during the study year by sex in the Eastern Health District of Baltimore, 1939-1940.[1]

chronic cases are considered, a slightly higher proportion of male cases had medical care; the reverse was true for "minor" cases of chronic illness.

When amount of care per attended case is considered, as shown in Table 5, females with a "major" chronic illness had considerably less care than did male cases in the same category. There was no difference in amount of medical care between the sexes for cases of chronic illnesses classified as "minor."

It may be concluded that both "major" and "minor" chronic illnesses were present in a considerably greater number of females than males in the population studied. On the whole, however, the

Table 5. Doctors' calls and clinic visits per attended case of chronic illness among males and females in the Eastern Health District of Baltimore, 1939-1940.[1]

Classification of Cases of Illness	Males	Females	Ratio of the Average for Females to That for Males
Total Cases of Illness[2]	9.1	6.8	0.74
Major Chronic	9.8	6.5	0.66
Minor Chronic	7.4	7.5	1.01

[1] The population includes 1,757 white families observed two months or longer.
[2] Illnesses included in the classes, "major" and "minor," are enumerated on page 226 of the text.

chronic illnesses reported for males were considerably more severe than those reported for females.

Incidence of Illness

Incidence in this report of morbidity expresses the rate at which attacks of illness occurred in the observed population over a period of twelve consecutive months and does not include illnesses present at the time of the first visit to the family. Acute attacks of chronic illness which occurred during the year of study are included. The attacks of illness have been classed into two broad diagnosis groups, respiratory and nonrespiratory. In order to insure a fair degree of comparability in the data for both sexes, female genital and puerperal diagnoses have been excluded from all tables, except appendix tables which are shown at the end of the report. The number of cases of male genital diseases was so small as to be negligible; such cases have not been excluded.

Table 6. Incidence of illness by sex during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.

Causes of Illness and Classification of Disability	Rate per 1,000 Population[1]		Ratio of Rate for Females to Rate for Males
	Male	Female	
All Causes[2]	1,105.0	1,593.9	1.44
Nondisabling	623.7	984.8	1.58
Disabling but not Confined to Bed	234.4	276.2	1.18
Confined to Bed	247.0	332.9	1.35
Respiratory Illness	669.7	915.2	1.37
Nondisabling	384.8	569.7	1.48
Disabling but not Confined to Bed	123.1	135.0	1.10
Confined to Bed	161.8	210.5	1.30
All Other Illness	435.3	678.7	1.56
Nondisabling	238.8	415.2	1.74
Disabling but not Confined to Bed	111.3	141.2	1.27
Confined to Bed	85.1	122.4	1.44

[1] The population includes 2,713 years of life for males and 2,770 years of life for females in 1,757 white families observed two months or longer.
[2] Excluding female genital and puerperal diagnoses. Excluding also cases of illness with onset prior to the study year.

Disability. The incidence from all causes of illness for females, excluding female genital and puerperal diagnoses, was 44 per cent higher than that for males; the rate for males per 1,000 population was 1,105 and that for females was 1,594. When these rates were further subdivided according to severity of the cases of illness, there were some interesting differences which are shown in Table 6. The rate for females exceeded that for males for each severity category, but the amount of the excess varied. The excess was greatest for nondisabling cases of illness; the rate for nondisabling illnesses for females was 58 per cent greater than that for males. For illnesses which were disabling but did not cause confinement to bed, the female rate was only 18 per cent greater than that for males. For bed illnesses, however, the female rate was 35 per cent greater than the male rate.

Since more than half the illnesses were classed as respiratory, and, therefore, the total rate might be unduly weighted by any characteristics of respiratory illnesses, the rates have been shown also in Table 6 for respiratory illnesses and nonrespiratory illnesses. It can be seen that the excess of illness for females over that for males followed the same pattern for each group of causes; the incidence of illness was higher among females than among males for each severity category, and the excess was greatest for nondisabling cases of illness, second for bed cases, and least for disabling cases not confined to bed. It is evident that the females had a considerable excess of illness over the males and that, when disability was used as a criterion of severity, there was an excess both of severe and minor illnesses.

The proportions of cases of illness in each disability group are compared for each sex in Table 7. Of the total illnesses for males, the per cent accompanied by disability of one day or longer was 43.6 as compared with 38.2 for females. When the cases of illness were classified according to respiratory and nonrespiratory illness, the proportions in each disability group were very similar to those for all causes of illness. Although the females had a higher level of illness and also of bed illness, the proportion of illnesses graded accord-

ing to disability as severe was greater for males than for females.

The larger proportion of disabling illness among males as compared with females may have resulted in part from an underreporting of nondisabling illnesses among males. The excess of nondisabling illness among females suggests that there may have been a more complete reporting of minor illnesses for females than for males. It was found in the Hagerstown study[10] that females who reported their own illnesses had higher sickness rates than females who were not informants. However, it was also found that females who were not informants still had considerably higher sickness rates than males. In this study, as in the Hagerstown study, the housewife was usually the informant. Undoubtedly, some part of the excess in the nondisabling illnesses for females may have resulted from the fact that they reported their own illnesses more

Table 7. Distribution of cases of illness by degree of disability and by sex in the Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Cases of Illness			
	Male	Female	Male	Female
	Per Cent		Number	
All Causes[2]	100.0	100.0	2,998	4,415
Nondisabling	56.4	61.8	1,692	2,728
Disabling but not Confined to Bed	21.2	17.3	636	765
Confined to Bed	22.4	20.9	670	922
Respiratory Illness	100.0	100.0	1,817	2,535
Nondisabling	57.4	62.2	1,044	1,578
Disabling but not Confined to Bed	18.4	14.8	334	374
Confined to Bed	24.2	23.0	439	583
All Other Illness	100.0	100.0	1,181	1,880
Nondisabling	54.9	61.2	648	1,150
Disabling but not Confined to Bed	25.6	20.8	302	391
Confined to Bed	19.5	18.0	231	339

[1] Based on 1,757 white families observed two months or longer during a period of twelve consecutive months.
[2] Excluding female genital and puerperal diagnoses. Excluding also cases of illness with onset prior to the study year.

[10] *Op. cit.*, footnote 2.

completely than those of males. However, it seems probable that the reporting of serious illness, especially cases resulting in confinement to bed, would be fairly similar for both sexes, regardless of the sex of the informant. The greater proportion of disabling illness for males than for females may result in part from an underreporting of minor illnesses, but it may also be indicative of greater severity of illness among males. In any case, no greater severity of illness among females as compared with males was evidenced.

Duration. In this study, another measure of severity which has been used is duration of illness. Table 8 shows the average duration of illness, disability, confinement to bed and to hospital for males and females according to each classification of disability. For nondisabling illnesses the average duration of each case was 21 days for males as compared with 23 days for females. For disabling illnesses not confined to bed, the average duration of illness for males was 24 days and that for females was 19 days. Of the total sick days for cases

Table 8. Average duration of sickness, disability, confinement to bed and to hospital for all causes[1] of illness by sex in the Eastern Health District of Baltimore, 1939-1940.[2]

Classification of Disability and Sick Days	Male	Female	Ratio of Average for Females to Average for Males
Nondisabling Illness			
Sick Days per Case	20.7	22.7	1.10
Disabling but not Confined to Bed			
Sick Days per Case	23.7	19.2	.81
Disabled Days per Case	12.9	9.1	.71
Confined to Bed			
Sick Days per Case	25.3	27.2	1.08
Disabled Days per Case	15.6	14.6	.94
Bed Days per Case	8.3	7.9	.95
Hospital Days per Hospital Case	12.2	15.6	1.28

[1] Excluding female genital and puerperal diagnoses. Excluding also cases of chronic illness with onset prior to the study year, but including sick days for all other illnesses with onset prior to the study year.

[2] Based on 1,757 white families observed two months or longer during a period of twelve consecutive months.

in this category, on the average there were 13 disabled days for males and 9 for females. The durations for bed cases were similar for males and females. There was an average of 25 sick days per bed case for males and 27 days for females. Each bed case incurred an average of 16 and 15 days' disability for males and females, respectively. The number of bed days per bed case was 8 for each sex. The average duration of hospitalization for each hospital case was 12 days for males and 16 days for females. The difference in the durations of illness for cases disabled but not confined to bed and especially the difference in the average duration of disability seem to indicate that the males may have suffered illness of greater severity than the females.

Medical Care. Severity of illness can be measured also by the medical care received, namely, by whether or not a doctor attended an illness, and if so, by the number of visits made. Table 9 shows for

Table 9. Per cent of illnesses receiving medical care by sex during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Per Cent of Illnesses Receiving Medical care	
	Male	Female
All Causes[2]	38.5	32.0
Nondisabling	22.3	18.7
Disabling but not Confined to Bed	48.1	39.7
Confined to Bed	70.3	65.0
Respiratory Illness	30.0	27.2
Nondisabling	12.1	12.1
Disabling but not Confined to Bed	40.1	36.1
Confined to Bed	64.9	62.3
All Other Illness	51.5	38.5
Nondisabling	38.7	27.7
Disabling but not Confined to Bed	57.0	43.2
Confined to Bed	80.4	69.6

[1] Based on 1,757 white families observed two months or longer.
[2] Excluding female genital and puerperal diagnoses. Excluding also cases of illness with onset prior to the study year.

males and females the proportion of illnesses which received medical care. The percentage of illnesses which received medical care among females was somewhat lower than that among males for each class of disability for all illnesses, whether respiratory or nonrespiratory, with the exception of nondisabling respiratory illnesses where the percentages were the same for both sexes. The difference between males and females in the proportion of illnesses receiving medical care was not large enough to be important for respiratory illnesses, but for nonrespiratory illnesses, the proportion among females which received medical care was 25 per cent less than among males.

When degree of disability is considered, the proportions receiving medical care followed the same general pattern for each sex, the highest percentage occurring for bed cases, the next highest for cases disabled but not confined to bed, and the lowest for nondis-

Table 10. Doctors' calls per case attended by a doctor by sex during twelve consecutive months, Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Doctors' Calls per Case Attended		Ratio of Average for Females to Average for Males
	Male	Female	
All Causes[2]	3.4	3.0	0.88
Nondisabling	2.6	2.3	0.88
Disabling but not Confined to Bed	3.6	2.7	0.75
Confined to Bed	4.0	3.8	0.95
Respiratory Illness	2.9	2.5	0.86
Nondisabling	1.9	1.9	1.00
Disabling but not Confined to Bed	2.5	1.7	0.68
Confined to Bed	3.6	3.0	0.83
All Other Illness	3.9	3.6	0.92
Nondisabling	3.0	2.5	0.83
Disabling but not Confined to Bed	4.5	3.7	0.82
Confined to Bed	4.7	5.0	1.06

[1] Based on 1,757 white families observed two months or longer.
[2] Excluding female genital and puerperal diagnoses. Excluding also cases of chronic illness with onset prior to the study year, but including all other illness with onset prior to the study year.

abling cases. The fact that a greater proportion of nondisabling illnesses among males received medical care than among females might be the result of an underreporting for males of minor illnesses which would not be likely to receive medical care. However, the greater proportion of disabling illness which received medical care among males as compared with females seemed to indicate a slightly greater severity of illness for males over females.

When the volume of medical care was considered in relation to the number of attended cases, Table 10, the males appeared to have a slight excess also in the average number of calls made to each case attended. The difference between the number of calls per attended case for males and females was not relatively large, but the difference was present for each classification of disability for all causes of illness. The average number of calls per attended case was higher for males than for females for respiratory and nonrespiratory ill-

Table 11. Clinic visits per clinic case by sex during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Clinic Visits per Clinic Case		Ratio of Average for Females to Average for Males
	Male	Female	
All Causes[2]	3.5	3.7	1.06
Nondisabling	3.4	4.0	1.18
Disabling but not Confined to Bed	3.9	4.0	1.03
Confined to Bed	3.4	3.2	0.94
Respiratory Illness	2.9	3.4	1.17
Nondisabling	2.1	5.7	2.71
Disabling but not Confined to Bed	3.9	1.7	0.44
Confined to Bed	2.6	2.1	0.81
All Other Illness	3.8	3.8	1.00
Nondisabling	3.7	3.4	0.92
Disabling but not Confined to Bed	3.8	4.4	1.16
Confined to Bed	4.0	4.0	1.00

[1] Based on 1,757 white families observed two months or longer.
[2] Excluding female genital and puerperal diagnoses. Excluding also cases of chronic illness with onset prior to the study year, but including all other illness with onset prior to the study year.

nesses with the exception of nondisabling respiratory cases, where there was no difference between the sexes, and nonrespiratory bed cases where the difference was relatively small. The calls per attended case were highest for both sexes for cases confined to bed. The excess of calls per attended case for males as compared with females might have resulted partly from visits of males to company doctors for nondisabling illness while at work, but for disabling illness, the excess seemed to indicate a greater severity of illness among males than among females.

When clinic visits per clinic case were compared for males and females in Table 11, there was relatively little difference between the sexes for all illnesses. The females had a somewhat higher number of clinic visits per clinic case for nondisabling illnesses. For bed illness, the males had a slightly higher average number of clinic visits for each clinic case. The number of cases of respiratory illnesses attending clinics was 80 for males and 83 for females so that considerable fluctuation in the averages according to degree of disability may have resulted from the small numbers. Very little difference between the sexes was noted in the average number of clinic visits per clinic case for nonrespiratory illnesses.

Volume of Medical Care

Another expression of the amount of medical care is the rate of doctors' calls and clinic visits per 1,000 population. The rates for each sex shown in Table 12 are based on all doctors' calls and clinic visits made throughout the year on account of illness and regardless of the date of onset of the illness. Medical care received for reasons other than illness, such as well-baby care, was not included in this report. The majority of the medical care calls were doctors' calls. Clinic visits formed 33 per cent of the total visits for males and 28 per cent for females. The rate of medical care calls per 1,000 persons was 1,968 for males, 2,220 for females, excluding genital and puerperal diagnoses, and 2,454 for females including care for genital and

puerperal diagnoses. It is interesting to note the similarity between these rates and those observed in the study of illness by the Committee on the Costs of Medical Care and the United States Public Health Service. Collins[11] reported a rate of 2,225 per 1,000 males, 2,474 per 1,000 females, and 3,054 per 1,000 females when care for genital and puerperal diagnoses was included.

The hospitalization rates for males and females are compared in Table 13. When the hospital admissions for female genital and

Table 12. Rate of doctors' calls and clinic visits for all cases of illnesses by sex in the Eastern Health District of Baltimore, 1939-1940.[1]

Medical Care and Classification of Disability	Rate per 1,000 Population[2]			Ratio of Rate for Females to Rate for Males	
	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
Doctors' Calls and Clinic Visits	1,967.9	2,219.5	2,454.2	1.13	1.25
Nondisabling	613.0	853.1	924.9	1.39	1.51
Disabling but not Confined to Bed	589.8	445.5	451.6	0.75	0.77
Confined to Bed	765.2	920.9	1,077.6	1.20	1.41
Doctors' Calls	1,322.2	1,602.9	1,805.1	1.21	1.37
Nondisabling	359.4	500.0	563.9	1.39	1.57
Disabling but not Confined to Bed	342.1	318.1	322.7	0.93	0.94
Confined to Bed	620.7	784.8	918.4	1.26	1.48
Clinic Visits	645.8	616.6	649.1	0.96	1.01
Nondisabling	253.6	353.1	361.0	1.39	1.42
Disabling but not Confined to Bed	247.7	127.4	128.9	0.51	0.52
Confined to Bed	144.5	136.1	159.2	0.94	1.10

[1] Includes all medical care given for illness during the study year.
[2] The population included 2,713 years of life for males and 2,770 years of life for females in 1,757 white families observed two months or longer during a period of twelve consecutive months.

[11] *Op. cit.*, footnote 5. The figures quoted exclude calls by nonmedical practitioners to agree with the Eastern Health District tabulation.

puerperal diagnoses are excluded, the female rate of 51 was found to be 25 per cent less than the male rate of 67 per 1,000. The total rate for females for all causes was 76 per 1,000. The institutional rates were 4.8 per 1,000 males and 4.0 per 1,000 females; the rate for females was 17 per cent less than that for males. If hospitalization may be considered a criterion of severity, the males again appear to have suffered more serious illness than the females. It should be pointed out, however, that hospitalization may not be an indication of the severity of illness so much as of the nature of the illness and of the treatment required; for example, a tonsillectomy with no complications may be hospitalized regardless of severity while, on the other hand, a relatively severe heart case may not be hospitalized because of an expected long duration and because of the type of

Table 13. Rate of hospitalization by sex during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.[1]

Classification of Hospital Cases	Male	Female	Ratio of Rate for Females to Rate for Males
	Rate per 1,000 Years of Life		
Hospitalized Illness[2]			
Excluding Female Genital and Puerperal Diagnoses	67.1	50.5	0.75
Including Female Genital and Puerperal Diagnoses	67.1	75.8	1.13
Institutionalized Illness[3]	4.8	4.0	0.83
	Number		
Years of Life	2,713	2,770	
Number of Hospital Admissions Excluding Female Genital and Puerperal Diagnoses	182	140	
Number of Hospital Admissions Including Female Genital and Puerperal Diagnoses	182	210	
Number of Institutional Cases[3]	13	11	

[1] Based on 1,757 white families observed two months or longer.
[2] Includes all cases of illness which had hospital care hospitalized at any time during the study year.
[3] Included also in "Hospitalized Illness."

treatment involved. In view of the evidence already noted indicating greater severity of illness among males than among females, it is interesting that the rate of hospitalization for males exceeded that for females.

Summary

The findings of the study may be briefly summarized as follows:

(1) The prevalence of illness was 62 per cent higher for females than for males.

(2) Chronic illness formed approximately 70 per cent of the total cases of illness present at any given time for both males and females.

(3) The proportion of cases of chronic illness which caused disability was higher among males than among females, and the proportion disabled throughout the period of observation was considerably greater among males than among females.

(4) There was no difference in the amount of medical care for "minor" chronic illnesses, but for "major" chronic illnesses attended cases among males received on the average 50 per cent more care per case than did female cases.

(5) The incidence of illness during the study year was 44 per cent higher for females than for males. The excess was greatest for nondisabling illness but was relatively high for bed illness.

(6) The proportion of attacks of illness which caused disability was greater for males than for females.

(7) The average duration of attacks of illness was similar for bed cases and for nondisabling cases for both sexes, but for cases disabled but not confined to bed, males had an excess over females both in total sick days and disabled days per case.

(8) A somewhat higher proportion of attacks of illness among males received medical care than among females, and the attended male cases received on the average more doctors' calls than did the females.

(9) Medical care expressed in relation to the total population indicated that there were 1.9 visits per male and 2.4 per female per year. Two-thirds of the total medical services were doctors' calls; clinic visits formed slightly less than one-third of the visits for both sexes.

(10) The hospitalization rate for males was considerably in excess of the rate for females when genital and puerperal diagnoses were excluded.

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Appendix tables will be found on pages 242-244.

Appendix Table 1. Rate of all illness by degree of disability and by sex in the Eastern Health District of Baltimore, 1939-1940.[1]

Classification of Disability	Rate per 1,000 Population[2]			Ratio of Rate for Females to Rate for Males	
	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
All Causes	1,279.8	1,845.5	1,945.1	1.44	1.52
Nondisabling	753.8	1,189.5	1,228.9	1.58	1.63
Disabling but not Confined to Bed	262.8	303.6	313.4	1.16	1.19
Confined to Bed	263.2	352.3	402.9	1.34	1.53
	Number				
All Causes	3,472	5,112	5,388		
Nondisabling	2,045	3,295	3,404		
Disabling but not Confined to Bed	713	841	868		
Confined to Bed	714	976	1,116		

[1] All illness includes both prevalence and incidence during the year's observation.
[2] The population included 2,713 years of life for males and 2,770 years of life for females in 1,757 white families observed two months or longer during a period of twelve consecutive months.

Appendix Table 2. Number of days of sickness, disability, confinement to bed and to hospital, and number of illnesses (all causes[1]) by sex in the Eastern Health District of Baltimore, 1939-1940.[2]

Classification of Sick Days and Cases of Illness According to Degree of Disability	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
Nondisabling			
Number of Sick Days	36,963	65,243	71,001
Number of Cases	1,785	2,874	2,938
Disabling but not Confined to Bed			
Number of Sick Days	15,805	15,304	15,818
Number of Disabled Days	8,586	7,292	7,398
Number of Cases	667	798	822
Confined to Bed			
Number of Sick Days	17,360	25,751	30,347
Number of Disabled Days	10,677	13,813	16,304
Number of Bed Days	5,702	7,518	8,828
Number of Cases	685	946	1,084
Hospital			
Number of Hospital Days	1,948	1,909	2,695
Number of Hospital Cases	160	122	191

[1] Excluding chronic cases of illness which had onset prior to the study year.
[2] Based on 1,757 white families observed two months or longer during a period of twelve consecutive months.

Appendix Table 3. Number of doctors' calls and number of male and female cases attended by a doctor during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Doctors' Calls			Attended Cases		
	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
All Causes[2]	3,201	3,755	4,279	940	1,237	1,347
Nondisabling	778	1,006	1,150	303	441	470
Disabling but not Confined to Bed	881	708	718	248	258	264
Confined to Bed	1,542	2,041	2,411	389	538	613
Respiratory Illness	1,399	1,550	1,550	479	627	627
Nondisabling	221	333	333	115	172	172
Disabling but not Confined to Bed	292	215	215	116	126	126
Confined to Bed	886	1,002	1,002	248	329	329
All Other Illness	1,802	2,205	2,729	461	610	720
Nondisabling	557	673	817	188	269	298
Disabling but not Confined to Bed	589	493	503	132	132	138
Confined to Bed	656	1,039	1,409	141	209	284

[1] Based on 1,757 white families observed two months or longer.
[2] Excluding cases of chronic illness with onset prior to the study year.

Appendix Table 4. Number of clinic visits and clinic cases by sex during twelve consecutive months in the Eastern Health District of Baltimore, 1939-1940.[1]

Causes of Illness and Classification of Disability	Clinic Visits			Clinic Cases		
	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
All Causes[2]	1,017	1,062	1,146	287	286	307
Nondisabling	375	485	505	111	122	131
Disabling but not Confined to Bed	374	293	297	97	74	76
Confined to Bed	268	284	344	79	90	100
Respiratory Illness	234	282	282	80	83	83
Nondisabling	42	182	182	20	32	32
Disabling but not Confined to Bed	106	22	22	27	13	13
Confined to Bed	86	78	78	33	38	38
All Other Illness	783	780	864	207	203	224
Nondisabling	333	303	323	91	90	99
Disabling but not Confined to Bed	268	271	275	70	61	63
Confined to Bed	182	206	266	46	52	62

[1] Based on 1,757 white families observed two months or longer.
[2] Excluding cases of chronic illness with onset prior to the study year.

Appendix Table 5. Number of doctors' calls and clinic visits of patients by sex with chronic conditions present at the time of the first visit to the family.[1]

Medical Care and Classification of Disability	Illnesses Present on the First Visit to the Family	
	Males	Females
Doctors' Calls and Clinic Visits	1,121	1,373
Nondisabling	510	907
Disabling but not Confined to Bed	345	236
Confined to Bed	266	230
Doctors' Calls	386	721
Nondisabling	197	412
Disabling but not Confined to Bed	47	176
Confined to Bed	142	133
Clinic Visits	735	652
Nondisabling	313	495
Disabling but not Confined to Bed	298	60
Confined to Bed	124	97

[1] The population includes 3,314 males and 3,336 females in 1,757 white families observed two months or longer during a period of twelve consecutive months.

Appendix Table 6. Number of doctors' calls and clinic visits for all causes of illness by sex in the Eastern Health District of Baltimore, 1939-1940.[1]

Medical Care and Classification of Disability	Male	Female (Excluding Genital and Puerperal Diagnoses)	Female (Including Genital and Puerperal Diagnoses)
Doctors' Calls and Clinic Visits[2]	5,339	6,148	6,798
Nondisabling	1,663	2,363	2,562
Disabling but not Confined to Bed	1,600	1,234	1,251
Confined to Bed	2,076	2,551	2,985
Doctors' Calls	3,587	4,440	5,000
Nondisabling	975	1,385	1,562
Disabling but not Confined to Bed	928	881	894
Confined to Bed	1,684	2,174	2,544
Clinic Visits	1,752	1,708	1,798
Nondisabling	688	978	1,000
Disabling but not Confined to Bed	672	353	357
Confined to Bed	392	377	441

[1] The population included 2,713 years of life for males and 2,770 years of life for females in 1,757 white families observed two months or longer during a period of twelve consecutive months.

[2] Includes all medical care given for illness during the study year.

A CONCEPT OF THE DEFICIENCY STATES[1,2]

H. D. KRUSE, M.D.

ALTHOUGH nation-wide dietary inadequacies have been revealed by surveys, the occurrence of deficiency diseases has not been generally noted except in city hospitals or endemic regions. Clinicians have asserted that they do not see deficiency diseases. This apparent discrepancy, despite much discussion, has remained baffling.

According to one explanation, many manifest cases are unrecognized. But even if these were detected, the figures on the prevalence of deficiency diseases would not match the data on the frequency of dietary inadequacies. Another explanation has been that deficiency diseases in an early or mild state are undetectable by ordinary clinical methods. This state was recognized in pellagra by Roussel who designated it incipient in preference to prodromal, latent, or larval (1). Recently it has been called subclinical.

This explanation raised two new questions. One was: By what means may deficiency diseases in this state be detected or recognized? Over the answer to this question there has been considerable division of opinion. The other was: What is the nature of deficiency diseases in this state? The views on this have been varied and vague. Yet it is a fundamental question, for its answer expresses a concept. Obviously, the prevalence of deficiency diseases that will be revealed depends on the methods of detection which are inseparably linked with the concept.

Study of the pathogenesis of deficiency diseases makes the existence of an early or mild state thoroughly understandable. A deficiency disease on a dietary basis develops in the following sequence: lowered concentration of the essential factor in the blood; depleted storage in the body's reservoirs; diminished excretion in

[1] From the Milbank Memorial Fund, New York.

[2] Presented at the Round Table on Nutrition, Twentieth Annual Conference of the Milbank Memorial Fund, May 7, 1942.

the urine; microscopic change in tissue; gross morphological and functional change. It is not to be inferred, however, that each step is completed before the next begins. The alteration in transport and storage and the microscopic change in tissue show that the disease does exist in a state which is undetectable by ordinary clinical methods. For most deficiency diseases these changes have been demonstrated by appropriate sensitive methods.

One line of evidence comes from biochemical methods in analyses of blood and urine. In avitaminosis C, for instance, low blood values for ascorbic acid have been found in a definite proportion of population samples (2, 3). True, some investigators have argued that such values for ascorbic acid in the absence of other signs do not constitute scurvy. Judged by clinical criteria, the condition is not scurvy. Not until it has advanced to macroscopic tissue changes and developed signs is it designated scurvy. But that view draws a purely arbitrary distinction. Its only justification is that it differentiates two states of severity in the process. One is the beginning or mild state; the other the fully-developed disease. But whatever the former is called, it is a step in the process. As a practical matter, it may call for therapy.

The other line of evidence on the existence of the early or mild state in deficiency diseases has been the demonstration of morphological changes. The early changes revealed by x-ray in scurvy have been described (4). Biomicroscopy has disclosed still more about the early and mild state of several deficiency diseases. Just as the microscope was highly useful to the pathologist in extending his range of vision to lesser changes in postmortem tissue, it has now proved highly informative to apply it in deficiency diseases to changes in living tissues. It is particularly revealing if the site showing very early changes is selected for observation. Kruse has found specific biomicroscopic changes for four deficiency diseases: avitaminosis A (5), ariboflavinosis (6, 7), aniacinosis (8), and avitaminosis C (9).

In this morphological study of these deficiency diseases, with biomicroscopic in conjunction with macroscopic examination, it was possible to see all gradations and to reconstruct the sequence of changes. These observations, combined with the results from administration of specific therapy, have clearly shown that the early or mild state has a deeper meaning than was previously recognized. While each of these four deficiency diseases was a separate and distinct entity and had its specific individuality in details, all showed a similarity in their general biological behavior. They seemed to reflect certain principles. Accordingly, they have formed the basis for a new concept of deficiency diseases, their evolution, the state in which they exist, how they may be recognized, and their response to specific therapy.

First, it should be stated, each avitaminosis shows a specificity and invariability of the particular tissue sites in which characteristic lesions appear. This point has been demonstrated over and over in animals and humans. For studying the evolution of each condition, a tissue site affected early and undergoing changes throughout the entire course yields most information. It is found that the pathological process manifests a definite sequence of changes in this tissue.

Whether developing or receding, a deficiency disease possesses certain properties. First, the pathological process in the tissue has velocity. In the beginning this is not a constant, but an increasing velocity, an acceleration. How rate behaves next cannot be definitely stated. Probably the process, having achieved its potential maximum velocity, moves ahead for a time with little change in it. Naturally, this rate would not be absolutely constant. These velocities are determined by the causal force[8] which in turn is a function of causal degree and rate. The causal force increases or decreases

[8] To many persons the term "deficiency disease" connotes a disorder arising solely from a deficiency in the diet. But a deficiency disease may occur without any inadequacy in the diet. True, dietary inadequacy is the most common cause; but there are many others.

(Continued on page 248)

according to these two factors. As counteracting forces go into action, the velocity of the process is slowed. Or with therapy, the pathological process undergoes deceleration, arrest, and reversal. But the maximum rate at which the curative force can act is governed by the rate at which the tissue process developed. The possible time schedules on which the process may evolve will be arbitrarily classified here into two main kinds, which are subdivided.

In the one, the pathological process in tissue is rapid in onset, in running its course, and in responding to therapy. For the process to have marked acceleration the immediate causal force must be considerable. Its magnitude depends on the degree and rate of the cause. For maximum effect this may be brought about by a sudden change from an optimum diet to one markedly deficient in an essential. Such a deficient diet, applied abruptly, causes the body to draw steadily on its reserves to compensate for deficit in intake. As the reserves increasingly fail to meet the demands, there is rapidly increasing deficiency in the body. Thus, there is increase in its intensity and its rate, an acceleration, which is reflected in its force. At the start, the tissue to be affected had a pathological rate of zero, or perhaps a negative value. Markedly increasing the force of the deficiency accelerates greatly and imparts a rapid velocity to the pathological process. It appears and progresses at a rapid rate. It

More properly, the term "deficiency disease" should connote a deficiency in the bodily tissues rather than in the diet. Indeed, its meaning should be even broader; it should include not only a deficiency but also any metabolic disturbance of the essential in the tissues. The causes of such a deficiency or disturbance are numerous and may be complex. They may be conveniently classified as external and internal. Dietary deficiency is the most common external cause. Any bodily condition interfering with digestion, transport or utilization, promoting destruction or excessive excretion, or raising the requirements of the dietary essential is an example of an internal cause. Almost every nonnutritional disease affects nutrition. A cause comes about through a combination of circumstances. For example, assuming a satisfactory internal mechanism, a deficiency disease may arise from insufficient intake relative to age, activity, exposure to light, storage, state of tissue, and probably other factors.

The innumerable chemical reactions and complex relationships in which the vitamins participate are just beginning to be appreciated. In full cognizance of their biological importance, it would nevertheless be inappropriate to attempt to bring into the present discussion these intermediate details. Rather, the broad aspects are sufficient for the present purpose, a consideration of the development of the deficiency states as manifested in tissue.

has characteristic manifestations reflecting this swift velocity. This is an acute process, an acute deficiency disease. With application of therapy in sufficient amount, the velocity changes similarly but in the reverse direction. The pathological process is decelerated and stopped; then the restorative process is accelerated. Pathological changes which have developed rapidly recede quickly. This acute process is rapid in development, progress, and recession.

There is another form in this acute category. Here the bodily deficiency occurs rapidly but becomes only slight or moderate in degree. Thus, it acquires a marked increase in rate but only slight intensity. This resultant is reflected in its force which is somewhat less than in the acute form. The pathological process is rapid but less rapid than in the acute form. It might be called subacute. Or, since it is mild in intensity, it might be designated mild acute.

The second main form of the process is slow in onset, progress, and response to therapy. Its development might be conceived as follows: For the process to have only slight acceleration the immediate causal force must be slight. This state may be brought about by a very slow change from an optimum to a moderately or markedly deficient diet. Such a deficient diet, applied very slowly, causes the body to draw very slowly on its reserves to compensate for the deficit in intake. As the reserves steadily fail to meet the demands, there is a slowly increasing deficiency in the body. Thus, there is an increase in its intensity, but at such a slow rate, over such a long period, that its force never becomes marked. Slightly increasing the force of the deficiency slowly accelerates and imparts only a slow velocity to the pathological process. It develops and advances at a slow rate. It has characteristic manifestations reflecting this slow velocity. This is a chronic process, a chronic deficiency disease. With application of therapy in sufficient amount and for a sufficient period, it gradually but completely recedes. The chronic form is slow in development, progress, and recession. The acute and chronic processes differ fundamentally in velocity.

Another form belongs in the chronic category. In this the bodily deficiency occurs very slowly and becomes only slight or moderate in degree. Its slight increase in rate and intensity is reflected in its force which is very slight and somewhat less than in the chronic form. The pathological process, more gradual than in the chronic form, is very slow. We have designated it mild chronic.

Time, a much neglected factor in malnutrition, operates in another way, namely duration. Here again the acute and chronic processes differ. Just as the acute process is rapid in rate, it is relatively short in duration. A few weeks out of a lifetime is almost infinitesimal. In these instances, time is almost zero. If uninterrupted, the acute process runs through a definite sequence of manifestations in a rather short time. It may, therefore, be divided into stages. Naturally, it may be interrupted at any stage and reversed to normal if the therapy is complete.

The chronic process, if uninterrupted, will run at its slow rate for a long period, in fact probably for life. During this time it progresses in a definite sequence. Therefore, it too may be divided into stages. In the past it may have been thought that a slight dietary deficiency prevailing even for years produced no tissue change. On the contrary, with persistence of a slightly deficient diet over years, the chronic process progresses with mild intensity in a definite course. This chronic process may be interrupted at any stage by therapy; but only adequate dosage and time bring complete reversal.

Besides its rate and duration, the pathological process also has intensity.. The intensity of the cause leads to a corresponding intensity of the lesion. Just as there may be all degrees of intensity in causation—for example, all degrees of a deficiency in the diet—so there are all degrees of resulting lesions. Actually, the number of degrees which would be expressed would depend on the units and scale arbitrarily adopted. For present purposes, it is sufficient to divide the gradient levels into two groups: (1) severe, which is suf-

ficiently marked to produce gross lesions, from the just perceptible to the most pronounced; (2) mild, which is of so low intensity as to produce changes perceptible only by microscopy.[4] These two categories, mild and severe, it will be noted, refer to actual tissue change, not to symptoms. They apply to both the acute and chronic processes.

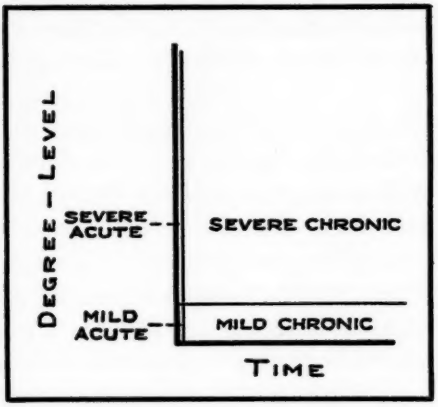

Fig. 1. States of a deficiency disease according to form, intensity, and stage. Divisions representing stages have not been indicated. From this chart the action of degree, rate, and duration of the cause in determining the tissue state may be visualized.

In considering the deficiency diseases in relation to intensity and time, it is evident that the acute and chronic states may be either mild or severe. Therefore, the simplest classification provides the categories: mild acute, mild chronic, severe acute, and severe chronic, with each divided into stages. The action of intensity, rate, and duration in determining the tissue state may be visualized from Figure 1. Divisions representing stages have not been indicated. Under this classification such a term as latent or subclinical state is no longer necessary. It is seen to be a broad state comprising the mild acute and mild chronic conditions. It is preferable to use the more specific designation corresponding to the actual condition.

Thus far we have presented the evolution and recession of the acute and chronic states in their simplest course: as if they arose in normal tissue and with therapy their cure was always complete.

[4] Actually, our system of rating now in use provides for four degrees of intensity for each stage in both the chronic and acute process.

But actually, in life, events are somewhat more complex. In the acute form there are several eventualities. It may run its acute course. With an untreated severe process, the patient either succumbs, or becomes inactive and has a poor appetite, both being protective mechanisms. In the latter event the process then advances at a slower rate. Or this first acute episode may be relieved by improvement in diet. But complete recovery, based on tissue restoration rather than symptomatic relief, would at best be slow because of the limited potency of food. If therapy is terminated upon relief of distressing symptoms or disappearance of late signs, response would be rapid but recovery incomplete. It is clear that as a result of any of these procedures, cure of the acute process would not always be finished. The recession in intensity, stage, and rate would not be complete. Consequently, the process would be brought to a new state with subsequent developments depending on circumstances.

With lapse from an optimum to a moderately deficient diet before recession was complete, the pathological process would resume at a slow rate. With a good diet following incomplete therapy, the process would remain stationary; with a slightly or moderately deficient diet, the pathological process would renew its advance at a slow rate. Also, an untreated mild acute process, running its course, would continue at a slower rate. As the result of any of these circumstances, the pathological lesion does not return to normal but persists on a lower level in the chronic state. Here it may be in equilibrium or progressing as a chronic process at a slow rate. In addition to arising from normal tissue, a chronic process may be seen to arise from an acute. Circumstances would again determine further developments.

By appropriate intervention this chronic process may be interrupted at any stage. But only by adequate therapy for sufficient time is its recession complete. In the event that a previously unsatisfactory diet is corrected, the chronic process becomes static or recedes very little and extremely slowly. Or with therapy for an in-

sufficient period, the process will recede incompletely. Thereafter, if the diet is slightly deficient, the slowly receding process may turn to a progressing chronic process. Or with a deficient diet and no therapy, the chronic process will continue its advance. Under these various unfavorable circumstances the chronic process, once contracted, may recede slightly, become stationary, or progress, depending on the diet.

The person with an arrested or chronic process may shift his diet from bad to worse and vice versa, but seldom to good. It is common knowledge that moderate or marked dietary deficiencies are apt to occur seasonally. They set up a mild or severe acute process, emerging usually in the spring. Other causes may act more infrequently but similarly from time to time. The arrested or chronic process constitutes a base on which this acute change is superimposed. To attain the same velocity, it takes less force to speed up an existing arrested or slowly moving process than to establish and then accelerate a process. Or, expressed in another way, a degree of dietary deficiency that would not produce an acute process in a well-nourished body would produce it in an already deficient body with a chronic process. Thus, an acute process may arise more easily from a chronic base. Under incomplete treatment the acute process disappears and leaves the chronic base, which may again undergo exacerbation. Repeated every year, this cycle is known as seasonal recurrence.

These do not represent all the possible changes in rate, stage, and intensity which a process may undergo. The diagram presenting the field suggests many more possible movements. The result is much more complex than was originally presented. But in sum, a mild or severe acute process in any stage may be seen on a mild or severe chronic form in any stage. These combined states add to the number of categories which must be borne in mind. It cannot be overemphasized that these combined states are very prevalent, perhaps the most prevalent.

The severe acute state is the form on which almost all clinical attention to deficiency diseases has hitherto been focused. Historically, this form, presenting a grave problem, was the first to be recognized; consequently, the recorded knowledge on the symptoms, signs, and pathology of this form predominate in the literature. Similarly, in experimental work, where the objective was to demonstrate the existence of new vitamins or to assay foods, animals were suddenly shifted from an optimum natural to a deficient "purified" diet in which every trace of an essential had been as far as possible removed. Naturally, the severe acute form of deficiency ensued.

In the past the mild and chronic states have received only sporadic and scant notice. By nature they have not been likely to attract attention. The mild are not conspicuous; indeed, they are below the level of unaided perception. Their associated symptoms, though often troublesome, are not so intense as to be unbearable or to necessitate medical consultation. Often the patient is unaware of symptoms until therapy has brought relief. The grossly perceptible chronic process comes on so gradually and insidiously as not for a long time to be obtrusive. Only in the advanced stages is it likely to draw complaint. Though noted often, little significance has been attached to it. Its relation to nutrition has been unrecognized.

Since the chronic state of deficiency diseases has not been commonly recognized, it is worth while to mention some of its characteristics. Its essence is time. For persons this is age. The longer persons live, the more chance they have to incur changes and to have them develop to an advanced state. Consequently, chronic changes are seen with greater frequency and in the latest stages with increasing age. This I have noted for avitaminosis A, ariboflavinosis, aniacinosis, and avitaminosis C.

In the past these chronic alterations have been called senile changes with the implication that senility causes them. But senility *per se* is not responsible for them. That has never been a satisfactory

explanation. Not all elderly persons show the changes. On the other hand, they occur in children. Time, not senility, is the essential point. And time does not start the changes, it simply is a dimension over which they progress. They are specific avitaminoses in a state of chronicity, due usually to respective dietary deficiencies running over a period of years. Their prevalence and severity vary with the number and degree of deficient diets and therefore with economic level. Most important of all, they are reversible, yielding slowly but completely to appropriate therapy.

This rate of response is another characteristic peculiar to chronic changes. Whereas acute changes respond with considerable promptness, chronic changes recede very slowly. In acute changes we are accustomed to expect improvement with dramatic rapidity. Actually, some of the rapidity is more apparent than real. For one thing, it is a relative matter; the more pronounced the acute, the more spectacular is a given degree of improvement. Often, removal of late signs constitutes supposedly rapid cure of an acute deficiency. Obviously, this is far from complete cure. But it is mainly because the relief of symptoms, the first event, is so prompt as to be striking. If judged solely by freedom from symptoms, the therapeutic response of acute is rapid. But when judged by complete restoration of all tissue changes, as seen by the biomicroscope, response in the acute condition is not quite so spectacularly quick as it is reputed. Nevertheless, response is very much more rapid in the acute than in the chronic state. The reason lies in the differential nature of their pathology. The tissue changes in the acute form of a deficiency disease are of a kind that appears rather rapidly and disappears just as readily. Those in the chronic form, with time allowing progression, are of a kind that progresses slowly and insidiously and recedes just as gradually.

Scattered observations in the literature on deficiency diseases are in accord with the concept presented here. The states are designated in terms identical with or similar to our nomenclature. In describ-

ing various forms of rickets, Eliot and Park mentioned: early mild, florid, and mild chronic (10). Their description of the course of these respective states may be interpreted in terms of intensity and time.

Furthermore, the literature records the characteristic difference between the acute and chronic forms in response to treatment. Eliot and Park remark that in one form of rickets the complete cure is slow (10). It has also been noted that in treatment of polyneuritis in animals, the acute fulminating type disappeared very speedily in a few days, the chronic type very slowly, in fact only after many months (11).

Even more significant has been the experimental production of scurvy in four states, depending on varying degrees of deficiency in vitamin C and the length of the experimental period (12). Tozer differentiated the chronic from the acute state on a time basis. She stated that the chronic form varies in severity according to the degree of deprivation of vitamin C. Indeed, using a different nomenclature to express intensity, she described mild and severe degrees for both the acute and chronic forms. Similar results have been reported on experimental vitamin B_1 deficiency (13, 14, 15).

Some broad generalizations can be drawn about these states in relation to factors affecting them. Like prevalence, the status of a deficiency disease is influenced by economic level, geographical region, and age, as well as by lesser environmental factors. Of these three it may be seen that the first two are indices of the number, nature, and degree of dietary deficiencies. Age is again the time factor. In the lower economic groups, deficiency diseases tend to be more numerous, more severe, and more advanced than in the higher economic groups. In geographical regions where a particular deficiency disease is endemic, the severe acute form is common; in other regions, it is rarely seen. If the disease is present in the latter, it is mostly in the chronic form. At younger ages, deficiency diseases are likely to be less prevalent and mostly in the mild acute or begin-

ning chronic state; at older ages they are apt to be more frequent and largely in the chronic form.

These influences are not invariable, absolute or completely decisive. Economic level and geographic region are far from perfect correlates of deficient diets; age does not initiate a deficiency disease. Nor are these influences of equal weight. Perhaps the most influential is economic level. But many persons in the higher economic groups do have severe deficiencies; while some in the lower miraculously escape. Only a small proportion of persons in an endemic region come down with an acute deficiency disease; almost all of these are in the low-income group. As for the influence of age, adults may be normal; whereas children, particularly if they are from low-income families, may exhibit a chronic process. We have seen numerous children from 8 to 11 years old with chronic changes similar to those most frequent in the middle-age group. But all these children were in the low economic group.

Obviously, the recorded prevalence of malnutrition depends on the concept, criteria, and means of recognizing it. In the recent past it has been judged by physical measurements or by presence of signs, including those of the acute severe type of deficiency disease. Neither method has revealed any considerable prevalence of malnutrition. It is very misleading to rely solely on them and to accept data only from them as evidence of malnutrition. Simple inspection is not sufficiently sensitive to detect very mild changes, whether acute or chronic. Most of the chronic changes, even when severe, have not been recognized as specific characteristics of deficiency diseases. These mild acute and mild or severe chronic conditions constitute the largest part of malnutrition.

As a means of appraising nutritional status, various new methods have been proposed for recognizing deficiency diseases. It is now plain that a method should detect and grade such a disease, whatever its state. The method should apply to both the acute and chronic forms, in all their stages and degrees. At once it should be stated

that the various new methods pertain to different aspects of a deficiency disease, yield dissimilar kinds of information, and are unequal in meeting the requisites.

For the appraisal of nutritional status, the biochemical determination of the concentration of a vitamin in the blood or urine, with or without a test dose, has very definite and narrow limitations beyond which it is misleading. In the evolution or recession of a deficiency disease, the blood and tissue changes are not synchronous. They are on different time schedules; they do not start simultaneously, nor do they proceed at the same rate. A shift in the blood value constitutes the first bodily change. The concentration of the vitamin in the blood changes much more rapidly than does the tissue process.

Values on the concentration of a vitamin in the blood reflect very sensitively the recent dietary habit (16) as well as other conditioning factors. They may change not only with season (17) but also within shorter periods; they may fluctuate. Hence, the blood values may temporarily be moderate or high without demonstrable improvement in an existing chronic tissue lesion (9). Indeed, there is much to indicate that sustained satisfactory blood levels resulting from conversion and adherence to a satisfactory diet are not accompanied by an appreciable recession in the tissue pathology.

Potent therapy will produce maximum blood levels and entirely restore bodily saturation in several weeks but will completely repair the slightest chronic tissue lesion only in months (9). Hence, the blood value may be high while the tissue pathology has yet shown little recession; the high blood level will be maintained over the many months while the tissue lesion is receding but is, of course, still abnormal.

In any of these events, the blood value would indicate a satisfactory nutritional status while the tissue would be pathological, a rather common occurrence. Manifestly, an assessment based on blood data alone would be erroneous.

It should be clear that there is no necessarily high correlation be-

tween data derived by different methods on the same deficiency disease. They provide information on different aspects and states of the disorder. Unfortunately, this fact has not been appreciated. Rather, it has been thought that various methods applied to the same deficiency disease should yield similar data. On this basis it has become the practice to test the validity of a method by comparing its results with blood values. This procedure is entirely unsound. When it is remembered that blood values shift rapidly and may fluctuate intermittently, while tissue changes very slowly, there should be no expectation of identical results.

The limitations of the blood methods for the evaluation of nutritional status cast no discredit. Used appropriately, they have their value. For following of dietary habits in the body, for secondary screening of persons without avitaminotic tissue changes, for specific metabolic studies, the blood technics are the methods of election.

The methods which embody gross and biomicroscopic examination of specific tissues for characteristic morphological changes—the eyes for avitaminosis A and ariboflavinosis, the gums for avitaminosis C, and the tongue for aniacinosis—meet most requirements for appraising nutritional status. Particularly, they permit both the acute and chronic forms in any stage and degree of tissue change to be detected. True, if the tissue is normal, it is possible that the blood values may be low. This situation, however, is the least frequent in the general population. Such a circumstance would be most frequently encountered in infants and preschool children. But tissue change is so prevalent over all age groups, and the biomicroscopic system as a primary screen is so sensitive in detecting its very early or mild form, that practically blood values as a secondary screen would add information in only a comparatively small number of instances.

Already the gross and biomicroscopic methods of examining tissue have yielded results indicating a high prevalence of malnutrition. Even in high economic groups, there are few people in abso-

lutely perfect nutrition. Yet these results are not surprising. Very few persons have consistently followed throughout life a diet satisfactory in all essentials, escaped the many other causes of malnutrition, or had complete recovery from any impairment of their nutrition. The older the person, the more opportunity he has had for some dietary lapse or adverse influence. Then too, the standard of perfection in the tissue is very exacting. And the biomicroscopic method is so sensitive that it is capable of detecting slight abnormalities. From all these considerations, the high prevalence of deficiency diseases is not unexpected.

Taken by and large, most of the malnutrition is chronic, with or without mild acute; some of it is mild, but much is rather severe. This condition too is understandable. Much malnutrition, with incomplete or no treatment, passes into the chronic form either as an arrested or slowly progressive process. The latter is not uncommon. Often faulty diets persist for long periods, even years.

This concept of the deficiency states has further applications. In all treatment of deficiency diseases, it shows the need to recognize the chronic state and to carry on therapy for a sufficiently long time. Otherwise, seemingly disappointing results may lead to erroneous and misleading conclusions.

Finally, it furnishes a plausible basis for the interpretation of any relation that may be found between nutrition and health and resistance to disease.

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THE LINGUAL MANIFESTATIONS OF ANIACINOSIS, WITH ESPECIAL CONSIDERATION OF THE DETECTION OF EARLY CHANGES BY BIOMICROSCOPY.[1,2,3]

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IN previous papers we have described methods for detecting ariboflavinosis and avitaminosis A by gross and biomicroscopic examination of the limbus and conjunctiva, respectively (1, 2, 3). This paper presents a preliminary report of observations on changes in the tongue in aniacinosis (nicotinic acid deficiency or disturbance) as seen in the gross and with the biomicroscope. The number of cases was sufficiently large to show all states of the lesions.

Following administration of nicotinamide as specific therapy, the tongue lesions in three persons have now almost completely disappeared, as judged by microscopic examination. Initially more severe, the lingual lesions in all twelve others under this therapy have markedly receded, in some nearly completely. These persons are still receiving the specific therapy, and their lingual manifestations are continuing to undergo recession. Control groups receiving ascorbic acid or vitamin A have had no improvement of their lingual lesions.

Gross and biomicroscopic examination of the tongue is an advantageous method of detecting all states of aniacinosis.

DESCRIPTION OF GROUPS AND PROCEDURES

Forty-nine adults, 19 to 46 years of age, were examined. Twenty-three of the persons were white females; three, colored females; and twenty-three, white males. The white individuals were from

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various racial stocks. None regarded himself as sick, and all attended work regularly. All except four received wages ranging from $69-95 a month; four received over $100 a month.

Their tongues were examined, prior to therapy, with the biomicroscope as well as in the gross. Both types of examination were conducted on the anterior three-fourths of the surface of the dorsum and edges.

Likewise, their gums in their labial aspect were examined grossly and microscopically; the angle of the mouth only grossly. Inasmuch as specific skin lesions have been traditionally regarded as an early manifestation of aniacinosis, the skin was examined, prior to therapy, in all persons with all grades of severity of lingual lesions.

Seventeen persons were selected at random to receive nicotinamide therapy. They presented various states of tongue lesions. The remainder, forming a control group, were given ascorbic acid.[4] Another group, receiving vitamin A, served as an additional control group.

The specific daily therapy, started on April 9, 1941, consisted of 200 mg. of nicotinamide in four tablets of 50 mg., each being given at an interval during the day. During the five work days, the therapy was taken in the presence of the dispenser; for over the week-end a supply was given to be taken home. None of the individuals was advised of the nature of his lingual condition. There was no suggestion to take other therapy, or to modify dietary habits.

The daily dosages of ascorbic acid and vitamin A for the control groups were 500 mg. and 100,000 I.U., respectively.

Among those receiving the nicotinamide therapy, two have since become unavailable through departure and could not be further followed. For similar reasons, seven from the control group had to withdraw. At regular intervals tongue examinations have been con-

[4] The ascorbic acid given to the control group was generously furnished by Mead Johnson & Company, Evansville, Indiana.

ducted on the groups receiving the specific and control therapy, respectively. For the former, these examinations will form the basis for terminating therapy.

Description of Lingual Manifestations

In the evolution and recession of its specific lesions, aniacinosis was seen to be similar in behavior to avitaminosis A (3), avitaminosis C (4), and ariboflavinosis (5). While each has its individuality as a separate and specific entity, all four avitaminoses have several characteristics in common. They reflect a definite, biological pattern. From this was elaborated the concept of deficiency states presented in the preceding paper (6).

There it was shown that in a deficiency disease the specific pathological process in a tissue is characterized by velocity, intensity, and sequence. Of the velocities occurring, the range may be classified into two principal categories, which are subdivided. The acute process is rapid in appearing, in running its course, and in responding to therapy. Somewhat less rapid is the subacute or mild acute process. Differing from these in velocity, the chronic process is slow in onset, progress, and response to therapy. Even slower is the mild chronic process.

Since the pathological process may be of any intensity, it is convenient to graduate the range in two degrees, mild and severe. Therefore, the acute and the chronic process may be either mild or severe. With grouping by form and intensity, the simplest classification of processes provides the categories: mild acute, mild chronic, severe acute, and severe chronic. These are the same groups that were enumerated in designating a process according to its velocity. Hence, the mild and severe states are seen to differ in velocity as well as in intensity.

If uninterrupted, the process manifests its changes in a definite sequence which may be divided into stages. Therefore, in each of the categories, it may be divided into stages.

Through the common vicissitudes, particularly over years, the process usually changes in velocity, intensity, and even direction. Most common of the eventualities, the mild or severe chronic state, once contracted, constitutes a base on which is superimposed a mild or severe acute state.

We have devised a system of appraising the condition of the tongue in aniacinosis which takes into account the form, intensity, and stage of the pathological process. First, it may tentatively be classified according to the two main categories: acute and chronic. Then from its degree, it may be characterized in intensity as well as more closely in form. Finally, its stage is identified. Actually, this system provides more and finer divisions of intensity than just mild or severe. For both the acute and chronic processes, intensity is gauged in three degrees. The resulting acute forms are divided into four successive stages, the chronic into five, each with its particular and identifiable characteristics. A stage may show features of the preceding and next phase, but it is judged by its predominant characteristics.

In using this system, the status of the process may be most readily judged by visualizing its position on the graph presented in the preceding paper. If acute and chronic processes are both present—as most frequently they are—they can be appraised separately according to their intensity and stage. From two coordinates, degree and time, the position of each in its respective zone may be located as a point. Status is designated by a combined dual rating.

In the present series of cases the tongue as a whole, as well as its elements, the filiform and fungiform papillae, showed changes. Some showed marked gross manifestations; others exhibited less pronounced but unmistakable gross changes; a few, exhibiting very little grossly, displayed definite alterations perceptible by biomicroscope. All forms and gradations in degrees, stages, and extent of the pathological process were represented, except the advanced stages of the severe acute type. Both by arranging them in a progressive

series and by interpreting the reverse sequence of changes upon therapy, the details in the pattern of the pathogenesis could be reconstructed and the course of events determined.

In the tongue and its papillae, various pathological changes appear in definite sequence. However, it should be emphasized that here sequence refers to appearance and that inasmuch as a succeeding manifestation emerges long before the preceding one has disappeared, both may be present concurrently. In the acute forms, vascular hyperemia and proliferation, hypertrophy, and then extinction occur successively in the papillae. The vascularity and hypertrophy of the fungiform papillae impart to the tongue the familiar stippled, then the strawberry aspect, depending on the degree and stage. Redness and swelling, marginal indentation, and then baldness manifest themselves in the tongue. In the chronic form, the stages of progression in the papillae are: vascular hyperemia and proliferation; infiltration; and atrophy. As the chronic process advances, the tongue itself shows fissures, crevices, and loss of substance, producing generally a thin tongue with marginal serrations. Usually, there is a preferential order of involvement of the two kinds of papillae: the fungiform precede the filiform in undergoing change.

Each stage of the pathological process manifests an intensity and extent corresponding to the degree of the cause. But it should also be cited that the same stage may not prevail over all the tongue; different sites may show different stages. Although the changes in each part follow the same pathological sequence, all parts may not be synchronously affected.

Instead, the regions tend to be affected in the following definite order: tip, anterior and antero-lateral edges, anterior and antero-lateral margins of the dorsum, anterior border of predominantly filiform zone, mid-dorsum. Considering that the fungiform and filiform papillae differ in their distribution over the tongue, it is seen that regions with the same predominant type do not undergo simultaneous change. In general, involvement appears first an-

teriorly and proceeds posteriorly. It is of particular significance to note the extent to which involvement has advanced; the extent of the predominant stage of the process; and the extent of the most advanced stage.

In presenting in some detail the sequence of pathological changes in both the acute and chronic processes, we will follow the arbitrary divisions of the rating scheme and describe the characteristics of the successive stages.

In the acute state fungiform papillae are red from their vascular proliferation, dilatation, and engorgement. To a lesser extent the same reaction is present in the filiform papillae, but their opaque tips mask most of the vascularity. With them as a background, the injected fungiform papillae impart to the tongue a stippled appearance. These changes range in degree from slight to marked: they are the more intense, the more pronounced the causal agency. Similarly, the extent of the affected area depends on the degree of the cause. The hyperemia appears in the papillae at the edges of the tongue and proceeds over the margins.

Then swelling, in addition to the redness, of the papillae appears. These changes may be restricted to the tip and margins of the tongue. Here the reddened and hypertrophic papillae may stand out conspicuously. In marked degree the papillae may become much enlarged.

Next the tongue itself shows redness and hypertrophy. If the process is mild or moderate, the tongue is covered in the middle, but red and smooth on the tip and margins. Although the present series of cases contained none of severe intensity in this stage, the picture has been repeatedly seen and recorded in acute pellagra. If the process is markedly intense, the tongue, deeply injected and deprived of its papillae, is red and smooth, a cardinal or bald tongue. It may be quite large from swelling and show the identations of the teeth.

Ulcers or erosions may occur on the tongue late in the process.

Usually they begin on the edges and may later appear on any portion of the tongue surface.

In the chronic state the first stage presents redness and swelling in the fungiform papillae. These manifestations are in proportion to the degree of the cause.

In the next stage these papillae are likewise hypertrophied. But as a distinctive feature they show beginning infiltration which partially obscures their vessels and thereby diminishes their redness. In the mild state the size of the fungiform papillae is only slightly increased. All the filiform papillae are present on the dorsum except where a small atrophic spot may be seen.

In marked degree the tongue is very thick and may have a slight yellowish cast. Everywhere the fungiform papillae are markedly hypertrophied, with marked infiltration masking the hyperemia. On the lateral margins the few fungiform present may be yellow. Some may be seen ruptured with their yellow contents released.

On the dorsum the filiform are also markedly hypertrophied. Both kinds of papillae are so similar in appearance—in size, shape, and color—that they may scarcely be differentiated. Elsewhere the filiform papillae may be entirely absent. Here and there are very small atrophic spaces which probably mark their previous site.

Late in this stage, the tongue with a mild degree of involvement may present the following additional changes: On the anterior edge at the midline the fungiform papillae are embedded; elsewhere on the edge they are hypertrophied, but less than on the dorsum. At the midpoint of the anterior edge and front part of the anterior margin the tongue is smooth because the fungiform papillae are embedded. Elsewhere on the edge and margin they may be partially embedded. Then the upper part of each papilla projects as a small mound above the surface; the remainder is embedded.

On the anterior dorsum the filiform papillae may appear as small hobnails with small nests of atrophic fusion. Or they may

show partial or complete fusion and atrophy. On the anterior margin they may be reduced in number by 50 per cent or more. Then they are slender, show only a little cornification at the tip and project only slightly above the surface. On the anterior edge few or no filiform papillae are present.

In slight degree there may be a small seemingly eroded spot in the midline at the anterior border of the filiform zone, where these papillae have undergone much atrophy or completely disappeared. It may also appear mid-dorsally. Or, extending down the midline of the dorsum is a slight longitudinal fissure. On its walls are several white hypertrophied fungiform papillae. Dorsally the longitudinal fissure terminates in a transverse fissure. In high degree, there may be multiple slight crevices containing a few fungiform papillae in bullous form. All these changes represent the beginning of the next stage.

In stage 3 the infiltration in the fungiform papillae may be complete, so that it masks their vascularity. Indeed, they appear almost or entirely white. Another distinguishing feature is a longitudinal fissure extending down the midline and usually containing several bullous fungiform papillae. Scattered crevices may also be seen on the tongue. Furthermore, on the dorsum the slightly hypertrophic filiform, without fimbriation or cornification, are not easily distinguishable from the fungiform papillae.

Fungiform papillae on the dorsum are much less hypertrophied in this than in the preceding stage. Their previous hypertrophy seems to have given way to beginning atrophy. On the edges of the tongue they are much flattened or completely embedded. Filiform papillae are missing, for the most part, from the anterior edge and margin.

In the higher degrees of this stage the same relationships prevail but all the manifestations are more pronounced. On the anterior margin many of the fungiform papillae have become spatulate in form. Marked infiltration veils much of their vascularity. More and

deeper longitudinal fissures are present. The deepest runs along the midline and may bifurcate the tongue at the tip to produce the so-called swallow-tailed tongue. The other fissures may be parallel to this. On the walls of the fissures may be seen bullous or spinous papillae which were once fungiform.

Few or no filiform papillae are on the anterior edge and margin. They are present on the dorsum and have increased diameters but less projection. In appearance they are quite similar to the fungiform in this stage.

Late in this stage, both kinds of papillae have undergone further change. In the low-degree tongue, linear groups of two or more markedly infiltrated fungiform papillae have united to form cords on the anterior margin. Filiform papillae on the dorsum present a mixed picture. In one area they may be slightly hypertrophic; in another they may show atrophic foci with fusion of two to six papillae. More frequently there are broad areas of marked fusion and atrophy.

In the high-degree tongue, the previously hypertrophied papillae on the anterior margin of the tongue have atrophied to their original size. These heavily infiltrated papillae have a distinct outline but are deeply embedded. Still later they are markedly fused. These changes also extend to all fungiform papillae on the dorsum. Likewise, the previously hypertrophied filiform papillae on the dorsum undergo still further atrophy. They are partially fused and project so little that the surface of the tongue approaches smoothness. These changes usher in the next stage.

In stage 4 atrophy of the papillae tends toward extensiveness and completeness. Consequently, the tongue becomes denuded and smooth. It becomes thinner, probably through loss of substance in the broad sense of the word. Any previous fissures diminish and disappear. The tongue becomes whitish, often with a yellow cast. There may also be heavy furring over the tongue.

On most of the dorsum the filiform papillae may be partially

atrophied and fused, but in scattered foci or small areas they may be completely fused. Complete atrophy usually occurs in a wide sector along the midline. This latter forms a low region. Or there may be complete atrophic fusion and flattening over the entire dorsum, forming a large depressed area. Near the lateral margins there may be narrow band-like areas of partially fused, slightly projecting filiform papillae.

On the anterior margin the fungiform papillae are variable. In some tongues they may not have reached the atrophic state. In others they may be only slightly atrophic. Or throughout the area they may be flat and not sharply discrete. They may also be embedded to such an extent that the surface is nearly smooth. There may be foci of markedly atrophic and almost completely fused papillae. Only a few filiform may be present. These are isolated islets of disorganized, fused, atrophic papillae. Or they may be absent. Then the zone may be so completely atrophied in certain foci that it is impossible to distinguish the type of papillae. Thus, the surface of the tongue tends to become denuded and smooth.

As areas of depression appear centrally on the tongue, fissures from the previous stage diminish and finally disappear. Hence, some tongues may show residual shallow fissures. The entire tongue is perceptibly thinner and less red than in the preceding stages. It may have a yellow cast or a heavy coat.

At the lateral edges some tongues may show loss of substance indicative of the next stage.

In stage 5 the same type of manifestations as in the preceding stage is seen, but the atrophic process has proceeded further. The lateral edges are thin or have eroded areas. By early workers the latter were called slashed edges. In some, this may amount to a considerable loss of substance. The entire tongue is thin, smooth, and white.

The fungiform papillae are embedded, in some instances fused, except in the mid-dorsum where a scattered few may be spinous in

shape and project strikingly above the smooth surface of the thin tongue.

It should be reiterated that an acute process may be superimposed on a chronic base in any stage. For example, a thin, smooth tongue with thinned and eroded lateral edges may become red and have hypertrophied fungiform papillae project mound-like above the surface on the anterior margin and mid-dorsum.

None of the persons showed any cheilosis or skin lesion.

Changes on Therapy

Upon administration of the nicotinamide daily there was recession of the acute and then the chronic process. The severe advanced acute stage of pellagra is known to subside rather rapidly. As might be expected where the acute was superimposed on a chronic process, the former disappeared first. Redness and swelling of the tongue and papillary hypertrophy diminished and disappeared before the chronic changes underwent substantial reversal.

Then occurred recession of the chronic lesions in reverse sequence of their pathogenesis. Thus, they receded in definite order: lessening, then disappearance of atrophy, fissures, and infiltration. Naturally, in any instance, the stage of the chronic lesion determines the nature and site of the first changes in repair. It is not unlikely that in tongues with severe chronic lesions, repair in each of the several pathological manifestations may be operating simultaneously. But cessation of the most recent manifestation may at first be the only one observable. Because the manifestations appearing early in pathogenesis have more pronounced and extensive development, their recession may at first be relatively so slight as to be unobservable. The response of the various stages to therapy may be described in a composite account.

The tongue in the advanced stages of the chronic process became thicker, possibly by regaining vascularity, tissue substance, and fluid. The rodent areas along the lateral edges filled. Furring, discoloration, and smoothness on the surface disappeared.

On the dorsum, the filiform papillae which were previously indistinct and atrophic began to reappear in small numbers. Later they appeared over the entire area and became somewhat discrete, though at first they did not project very much above the surface. Thus, they gradually resumed their orderly arrangement. Still later they returned further to their usual shape and projected somewhat more above the surface. With the process, depressed areas or sectors filled. Also, the restoration of the papillae covered any denuded surface.

On the anterior dorsum, the fungiform papillae which had previously been partially or completely embedded began to project above the surface. Those which had been white now showed redness due to resorption of the infiltrate. Fungiform papillae which had been hypertrophied now diminished in size. At this point the filiform papillae on the anterior margin might still be completely fused. Often the filiform papillae in and adjacent to the area occupied by the fungiform were the last to show recovery, particularly if the fungiform were hypertrophied.

Fissures, especially prominent in stage 3, began to fill. Bullous papillae on their walls diminished and disappeared. Atrophic sectors or spots flanking the course of the fissures showed increased discreteness of the filiform papillae. After one year's therapy some fissures as well as most crevices already have entirely disappeared.

Elsewhere in this stage the hypertrophied fungiform and filiform, previously so similar in appearance, rather soon began to return to their usual dissimilarity. Resorption of the infiltrated material in both removed much of their hypertrophy and left the reddish fungiform in sharp contrast with the gray filiform papillae. Consequently, they could again be readily differentiated.

Tongues in the earlier stages showed the following response to therapy: In all zones the hypertrophied fungiform papillae diminished in size and assumed a reddish tint due to withdrawal of infiltrate. In atrophic areas on the dorsum, filiform papillae reappeared,

at first with slight, later with more discreteness and projection. Small areas near the anterior margin were usually the last foci to have the filiform papillae restored.

It should be noted that the criteria of complete recovery are rigorous since they are based on microscopic observations. After receiving therapy for fourteen months, three persons with their tongues showing almost complete restoration are near discharge. Several more are not far from complete recovery and discharge; all others have shown very marked improvement. In every instance the point to which the tongue has receded is in proportion to its stage before therapy. Naturally, the less advanced are among the first to show complete recovery. Nevertheless, they have required more than a year's intensive therapy.

Control groups receiving ascorbic acid or vitamin A have shown no improvement in their tongues.

Following the full recovery of those still receiving nicotinamide therapy, there will be a further report.

Discussion

Since pellagra results from a deficiency or disturbance in nicotinic acid, it is natural to ask what is the relation of the tongue changes to the disease. To find the answer it is helpful to trace the gradual change in views on the pathogenesis and diagnosis of pellagra. Then, through the concept of deficiency diseases and their detection, we may place tongue changes and pellagra in their proper positions and perceive their relationship.

Pellagra is a deficiency disease characterized by gastrointestinal disturbances, skin lesions, and sometimes neurological and mental manifestations. To the early investigator the disease showed so many manifestations and seemed so varied in evolution that it presented difficulties in characterizing its components. Each could be predominant. It was debated whether these many manifestations represent several types of pellagra or several stages of one type.

Lombroso wrote about types of pellagra, designating each by its predominant manifestation (7). Procopiu also classified pellagra into types according to the prevailing signs (8).

By almost all others, however, pellagra was recognized as an entity, though its manifestations were not restricted to one organ or system. Diverse systems were involved; not all were affected simultaneously, nor with the same intensity. Consequently, much discussion centered on whether pellagra developed in a definite and orderly progression, whether its several manifestations appeared in sequence. If so, the disease could be divided into stages based upon the predominant manifestations.

On this, there was much difference of opinion. Frapolli was the first to advocate division of pellagra into stages (9). Others subscribed to the validity of stages but suggested different divisions of the manifestations (10-15). Strambio based his stages not on predominant manifestations, but on the persistence or recurrence and the severity of the disease (16). More properly his stages should have been designated forms and degrees.

Others objected to division of pellagra into stages. Lombroso regarded it as artificial and inaccurate (7). Marie (17) asserted: "... the evolution of pellagra in a given case is not so logical as to have one stage succeed another. In a general way, it may be affirmed that the so-called first stage has reference to the gastro-intestinal and skin symptoms; ... As a rule, pellagra is a chronic affection and the duration of each stage is indefinite. Furthermore, the line of demarcation is not well defined between the different stages."

Roussel, whose writings on the evolution of pellagra are classic, concurred in this (18). In his opinion, the infinite variety in the course, duration, and gravity of individual cases vitiated all attempts to measure the progression of pellagra by phases, periods, or stages.

Several investigators divided pellagra into degrees according to its intensity (19-21). Roussel adopted the system of classification

into degrees but on a basis that only in part pertained to intensity (18). Despite his objection to dividing the disease into stages, his system of degrees was founded on the sequence of manifestations and grouping according to the predominant signs. Actually, his degrees were largely stages.

Commenting on the several systems of classification, Cazenave and Schedel (22) wrote: "The division of pellagra into commencing, confirmed and inveterate, is not a practical one, for pellagra may be beyond hope from its commencement. The expressions period or degree, which convey the idea of certain fixed symptoms and appearances, are not adapted to the description of a disease so capricious as pellagra. The term degree seems to indicate an increasing intensity; while the second or third time of appearance of the disease may be less severe than the first. When we employ these terms, therefore, we shall use them only as symptoms of a more or less advanced step of the disease; for, like every other disease, pellagra has a beginning, a progress, and a termination."

It may now be seen that all the classifications were open to criticism. Terms were used loosely or synonymously; they would indicate one basis of classification when another was actually used. Very often the system of classification was on a mixed basis. None was sufficiently comprehensive. They would have division on the basis of intensity to the neglect of stage, or vice versa.

The difficulty of the early workers in evolving a satisfactory method of classifying the various manifestations into stages is understandable. Their mistaken view on the etiology of pellagra colored their view on its nature and course. Many looked upon pellagra as a toxic disease and they expected it to fit that pattern. At that time they could not know that pellagra was a deficiency disease which may have a course very variable and quite different from that of a toxic or infectious disease.

Whether they sought to distinguish stages or degrees, all wanted to know the course of pellagra. They wished to recognize its se-

quence in order to know how far advanced were particular states. They also wished to know the earliest stage and its characteristics. Many systems of classification into stages or degrees included a prodromal period or an incipient pellagra (9, 10, 11, 13-15, 18, 23, 24). Even as early as 1866 Roussel, in mentioning his interest in early diagnosis, stressed the importance of discovering the site of initial change (18).

How many and what signs are necessary for diagnosis of pellagra was a topic under consideration even at that time. For all signs to appear, the disease would have to run its entire course. But, obviously for early diagnosis, all signs cannot be expected. That inescapable conclusion raised several kindred questions. How far must the process have developed before diagnosis may be safely made? How early may it be detected? What are the first valid signs? Roussel's distinction between the beginning and confirmed states, his use of the term confirmed, and his implicit acknowledgment that skin lesions were necessary to confirm the diagnosis, foreshadowed the trend in attitude which has since prevailed.

Perhaps because skin lesions were so prominent, they came to occupy the principal place among the signs. While other features were recognized, the dermatitis was given such weight as to overshadow them. It even preempted the name of the disease. Its presence was regarded as necessary for diagnosis. After it had become the decisive diagnostic factor, it alone was soon regarded as sufficient for diagnosis, and as the first reliable, valid sign.

Yet, several investigators have stated specifically that first changes do not occur in the skin; that other manifestations precede (12, 13, 15-18, 24-27). Indeed skin changes may be absent in pellagra, as was noted under the paradoxical term pellagra sine pellagra (7, 8, 16, 28). Sandwith (24) wrote: "The skin eruptions, although the least important of the various symptoms, have given the disease its name, and have always received an undue amount of attention."

Several experiments on exposing various parts of the body to the

sun while protecting other parts (19, 29, 30) suggest the circumstances under which the cutaneous lesions appear. Lavinder and Babcock (17), summarizing this, write: "... granting that the exanthem may ... develop more slowly, the skin is none the less affected in the shade, but sunlight intensifies the eruption, and it is not to be denied that the rays of the sun are thus an exciting cause of the skin lesions. ..." Perhaps, like night blindness in avitaminosis A, skin changes in pellagra are provoked, aggravated, or exaggerated by light, although they would emerge later spontaneously.

In any event, dermatitis is not the first change; indeed, it may not be present. It is not a *sine qua non* for diagnosis; certainly it is not a constant and reliable sign for early diagnosis. Nevertheless, dermatitis has remained unduly emphasized and in its absence many refuse to diagnose pellagra.

Several investigators have stated that beginning pellagra is characterized by gastrointestinal disturbances (8, 12, 13, 15, 18, 23, 24, 27), and the first observable tissue change is in the tongue (12, 15, 18, 25, 26, 27). Accordingly, it may well be asked: Can aniacinosis be appraised by changes in the tongue? Are specific changes in the tongue indicative of pellagra? Can early or mild pellagra be diagnosed by this specific glossitis alone? What is the relation of pellagra to aniacinosis?

For usefulness in the recognition of early pellagra and aniacinosis, any sign must meet certain criteria. It must always occur, be specific, and appear early. Since it is necessary to detect aniacinosis in all forms, degrees, and stages, and it is most convenient to use one manifestation which reflects all these, it is essential that the sign not only appears early, but persists and changes in proportion to the progress of the disease. It must be readily accessible to demonstration, preferably by an objective method.

By its never-failing occurrence in human pellagra, glossitis was shown to be a reliable sign. Even those who did not regard it as the

first sign, mentioned its presence. Furthermore, glossitis has been produced in experimental animals on B complex (31) or nicotinic acid-deficient (32-36) diets. Both the experimentally-induced glossitis in animals (37-39) and naturally-occurring glossitis in human pellagrins (40-42) have been cured by nicotinic acid. Moreover, in the last decade numerous endemics of glossitis, with or without angular stomatitis, have been reported (43-51). Gradually, the nature of the specific deficiency responsible for the occurrence of the glossitis was identified, as yeast (48-49) autoclaved yeast (50, 51) autoclaved alkaline yeast (52) and finally nicotinic acid (53, 54) were found to improve and cure it. From these lines of evidence, glossitis is seen to be a specific sign of pellagra and aniacinosis.

As the earliest presenting tissue change in pellagra, glossitis has been repeatedly reported in the past (12, 15, 18, 25, 26, 27). More recently it has likewise been recognized as the earliest discernible tissue manifestation (55-56). The occurrence of endemic glossitis further attests to its priority (43-51). The prevalence of tongue changes in the present series, with absence of other signs of aniacinosis, furnishes additional evidence. All this is not to say that glossitis is the first change in the body in pellagra and aniacinosis. Rather, among the readily observable objective signs, it is early, if not the earliest.

There has been some question whether the early specific changes in the tongue are indicative of pellagra. Its corollary is the question whether early or mild pellagra can be diagnosed by the specific glossitis. Among many clinicians, admitting that skin lesions were not first, strong tradition has made them reluctant to make a diagnosis of pellagra until skin lesions have appeared. Most of those who agreed that the first observable tissue change is in the tongue, skirted the issue by stating that this change characterized latent, prodromal, or beginning pellagra (15, 18, 26, 27). Even yet the person with typical tongue changes is not said to have pellagra. The matter is circumvented by calling glossitis a "pellagrous tongue," or

a sign of prepellagra (56). Quite general is the attempt to preserve the historical conception and designation of pellagra in contradistinction to its earlier states. Actually, however, they are only different states of one and the same process.

Perhaps the concept presented in the preceding paper (6) may help to locate the place of pellagra in aniacinosis. There it was shown by the simplest classification, a deficiency disease may exist in any one of the following states: mild acute, severe acute, mild chronic, severe chronic, as well as mild or severe acute superimposed on mild or severe chronic, each in a particular stage. It may be seen that aniacinosis, arising from deficiency of nicotinic acid, or of a chemically related compound that is its biological equivalent, or from disturbance of its metabolism in bodily tissue, covers all forms, degrees, and stages. Pellagra represents the severe degree and advanced stage of the acute form. This concept helps to relate the various manifestations in the tongue to respective states of aniacinosis; to clarify events in the ofttimes tortuous course of aniacinosis; and to emphasize the different rates of response to therapy according to the forms.

Most of the literature on pellagra is on its acute severe form. In these accounts the nature and sequence of tongue changes in acute pellagra have been abundantly reported. But it should be borne in mind that the acute severe form of aniacinosis may be engrafted on a mild or severe chronic base. Careful examination indicates that some manifestations of the tongue attributed to the acute state are actually characteristic of the chronic state. Either the acute process in the tongue was becoming chronic or, more likely, an exacerbation arose on a chronic base.

Pellagra has been called a chronic disease (8, 17) because its onset was often lengthy and its long course was punctuated by periodic and recurrent exacerbations. Several other investigators mentioned a chronic state, in contradistinction to the more dramatic acute form (11, 16, 57, 58). Relatively, however, chronic pellagra as a

distinct form has had little recognition. Some changes in the tongue have been described erroneously as part of the acute process, whereas they are really chronic in nature. Soler (59) and Lussana (13) mentioned fissures and coated tongue. Others cited furrows, smoothness, and yellow coloration (7, 18, 60).

In a notable paper emphasizing the importance of the tongue in diagnosis of pellagra, Gemma in 1872 wrote a comprehensive and detailed description of the lingual changes in pellagra (25). He described characteristics of the various lesions and tried to relate them in succession. Most of his affected persons, however, had acute changes on a chronic base. Since he drew no distinction between the acute and chronic forms with their respective manifestations, the sequence of changes which he recorded bears revision. Nevertheless, his characterizations of the tongue lesions are superb; most of them were seen in the present study; and much that he says about them, particularly his descriptions of the tongue in the course of the disease, and in the "cured" or arrested state, and in supposedly well adults and children, can be interpreted in the light of present work. It is significant that he noted the similarity between certain pellagrous and so-called senile changes in the tongue.

In the past some attention has been given to mild acute pellagra and its tongue changes. But the mild chronic state has gone almost entirely unrecognized. The lingual changes in the mild and severe states are similar except in degree. The most common states, acute with chronic, have not been fully appreciated as such and have not had their two constituent forms distinguished and separated. The present work supplies information on these forms, stages, and degrees as well as on the severe states. All the evidence indicates that tongue changes are present in all states of aniacinosis.

Two further points bear upon the recognition of the various states in relation to criteria and length of time for complete therapy. Many descriptions of pellagra have stressed its tendency to recurrence and periodicity (7, 8, 10). It is not unlikely that these pheno-

mena are associated with its chronicity. Usually relief of symptoms or clearing of skin lesions has, in the past, been regarded as the index of complete recovery and the signal for termination of therapy. In such a practice, judged by criterion of perfection, recession in the tongue would not be complete and therapy will have been prematurely stopped. The tongue is probably brought to a lower level of intensity to become a chronic base. This chronic base may undergo periodic exacerbation. Actually, recurrence has meant the return, not of aniacinosis, which is already present in a chronic stage, but of acute pellagra. As Katzenellenbogen so appropriately says in his paper on the cure of endemic glossitis (54): "To prevent relapse nicotinic acid must be administered for a long period."

In treating endemic glossitis with nicotinic acid, 50 mg. four to six times a day, Katzenellenbogen (54) noted considerable improvement in twenty-one out of twenty-four persons. With nicotinic acid, Aykroyd, Krishnan, and Passmore (53) observed improvement in sixteen out of twenty-four persons. The unsuccessful instances, though in the minority, are worthy of note. Katzenellenbogen does not mention the length of the therapeutic period for his apparently unimproved patients. When it is considered in the series of Aykroyd, Krishnan, and Passmore that fourteen persons received only maintenance doses and that many received therapy for only one week or less, a few for two weeks, and one who received it for twenty-six days had malaria concurrently, their results are surprisingly favorable. In the light of the present paper, which reveals the long period of therapy that may be necessary, depending on the state of the aniacinosis, it is likely that in both studies the length of the therapeutic period for the unimproved persons was too short. Moreover, in the one study, the dosages could not be considered sufficiently potent. The principle that a long period of therapy is necessary for recession of chronic changes is particularly applicable to the study by Alport, Ghalioungui, and Hanna (61) in which they reported that nicotinic acid was only

slightly effective for a chronic pellagrous process in the tongue. In chronic states, the therapeutic response is slow and a very lengthy period is required for complete recession.

From the preceding paper (6) it will be noted that the concentration of a vitamin in blood changes sooner and much more rapidly than does the tissue state, both in evolution and recession of a deficiency disease. Blood is the labile transport system with its concentration of a vitamin responding rapidly to change in intake. In the initial attack of the deficiency disease, the lowered concentration of the vitamin in the blood would be the first demonstrable change to be followed shortly thereafter by tissue change. For a short time, the tissue would be normal while the blood value would be low. But practically this condition is the least frequent in the general population, and is found mostly in infants and preschool children. Furthermore, it should not be forgotten that the biomicroscopic examination of tissue is exceedingly sensitive in detecting the very early and mild tissue changes, indeed all states.

Once chronic changes have appeared—and this is the most prevalent state—the blood values may be unreliable and misleading. The chronic process in the tissues recedes very slowly. In contrast, blood values shift rapidly in reflecting changes in intake, such as from seasonal or occasional dietary improvement or low potency maintenance tablets now so popular, and may temporarily be moderate or high without demonstrable recession in the existing chronic lesion. Even prolonged adherence to a good diet would not bring appreciable recession in the chronic process, while the blood values would be regarded as satisfactory. In all these instances, the blood values would obviously be misleading.

Examination of the tongue meets the criteria for satisfactory detection of aniacinosis. It is available to objective observation. Its changes are specific and invariable in occurrence. They are present in all states of aniacinosis; they appear early, persist, and reflect its course. They permit rating of any state in terms of form, stage, and

degree. It should be noted that stages were used historically in pellagra entirely differently than here. Then almost all the cases were exceedingly severe and well-advanced with several signs, each from a different system, in evidence; the stages were divided according to the predominant sign. In our rating different affected systems are not used as stages; rather the sequence of changes in one tissue. It is interesting that both Lussana (13) and Gemma (25) asserted that from the tongue alone they could identify the stage of pellagra.

Although very much may usually be seen in the gross, the biomicroscope is useful in detecting tongue changes. Very early stages and mild degrees of the process may be observed. It allows low-grade states, whether prolonged or not, to be detected. The less severe the change and the closer it approaches perfection, the more the microscope is needed.

Considerable evidence shows that there is high prevalence of aniacinosis (62). This is understandable. Relatively few persons have eaten a diet entirely adequate in niacin day after day throughout their life. The older the person, the more opportunity he has had for the dietary lapse. Similarly, any of the manifold deleterious causes contribute to impairment. The tongue shows cumulative changes, an arrested, incompletely receded, or progressive chronic as well as an acute process. Then too, the standard of perfection is very exacting and biomicroscopic detection is very sensitive. It is not surprising, then, that high prevalence of aniacinosis is found.

For complete recovery of chronic aniacinosis a long period of therapy is necessary. The acute form disappears, then the chronic process gradually recedes. In respect to response to therapy, aniacinosis is entirely similar to avitaminosis A, ariboflavinosis, and avitaminosis C.

The prevalence of much chronic aniacinosis, the long period of therapy required for its recession, the practice of treating acute

aniacinosis, including pellagra, for only a short time, all these suggest that in the past these states have not been completely corrected. Customarily, pellagra is treated until skin lesions or distressing symptoms disappear. To be complete the therapy should be continued until the tongue shows no abnormality. If therapy is then withdrawn, as it should be, pellagra will not, of course, be prevented in the future unless the diet remains adequate. But even if proper diet is not taken, complete cure will greatly postpone a recurrence.

The use here of 200 mg. of nicotinamide daily is not to be construed as a recommendation or precedent that this amount is necessary for maximum rapid therapeutic results. It is known that the effective therapeutic dosage for an acute avitaminosis is at least five to six times the maintenance requirement. It may be that a somewhat lesser dosage, but still above the dietary level, would suffice for a chronic avitaminosis, but that is yet to be demonstrated.

Summary

Of forty-nine persons in a low-income group, all had gross or microscopic lingual lesions characteristic of aniacinosis.

Following administration of nicotinamide to fifteen persons in this group, the lingual lesions in three have now almost entirely receded, as judged in all instances by biomicroscopic examination. The initially more severe lesions in the others of the therapeutic group have receded markedly, some nearly completely.

In all cases the striking feature is the very long period of time required for complete recovery, more than a year even with therapy of high potency. The type of pathology makes it understandable. In this respect, aniacinosis is similar to avitaminosis A, avitaminosis C, and ariboflavinosis. This common feature, the slow response, leads to a concept of malnutrition in which the importance of chronicity, as well as mild states, is emphasized.

Those persons receiving vitamin A or ascorbic acid have shown no improvement in the tongue.

For detection of aniacinosis, examination of the tongue is recommended as a simple, convenient, objective method. When biomicroscopic is combined with gross examination, all forms, degrees, and stages of aniacinosis may be noted and graded.

The marked prevalence of aniacinosis is explained.

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THE GINGIVAL MANIFESTATIONS OF AVITAMINOSIS C, WITH ESPECIAL CONSIDERATION OF THE DETECTION OF EARLY CHANGES BY BIOMICROSCOPY [1, 2, 3]

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IN previous papers we have described methods for detecting ariboflavinosis, avitaminosis A, and aniacinosis by gross and biomicroscopic examination of the ocular limbus, conjunctiva, and tongue, respectively (1, 2, 3, 4). This paper presents a preliminary report of observations on changes in the gums in avitaminosis C as seen macroscopically and biomicroscopically.

Following administration of ascorbic acid as specific therapy, the gingival lesions in two persons have now almost completely disappeared, as judged by microscopic examination. In all others, the gum lesions initially more severe have markedly receded under this therapy, in some nearly completely. These persons are still receiving the specific therapy, and their gingival lesions are continuing to undergo recession. Control groups receiving nicotinamide or vitamin A have had no improvement of their gingival lesions.

Gross and biomicroscopic examination of the gums is an advantageous method of detecting all states of avitaminosis C.

DESCRIPTION OF GROUPS AND PROCEDURES

Forty-nine adults were examined, and the personal details about them were presented in the preceding paper (4).

Their gums were examined, prior to therapy, with the biomicroscope as well as in the gross. Both types of examination were restricted to the labial aspect of the upper and lower gums between

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[3] Assistance by the Work Projects Administration for the City of New York, Official Project No. 65-1-97-21, W.P. 24, "Medical Evaluation of Nutritional Status," is gratefully acknowledged.

the first premolars on each side. Although Salle states that in adults the purely scorbutic gingivitis begins mostly on the anterior surface of the gums in the region of the incisors (5), our selection of this site was also determined by feasibility and convenience. It may be that lesions elsewhere in the gums appear first or are more severe, but changes are so prevalent in the frontal aspect that restriction of the examination to that site has proved practical and satisfactory.

The tongue, angles of the mouth, and skin were also examined as already described (4).

Thirty-two persons were selected at random to receive ascorbic acid therapy.[4] They had various states of gum lesions. The remainder, forming a control group, were given nicotinamide. Another group, receiving vitamin A, served as an additional control group.

Each of sixteen persons in the ascorbic acid group was given a capillary resistance test by the method of Schultz (6) before the therapy was begun. On each of twenty-seven persons to receive ascorbic acid and fifteen to receive nicotinamide a determination for the concentration of ascorbic acid in plasma by the macromethod of Mindlin and Butler (7) was conducted prior to therapy. Two months after therapy had been started, determinations for the ascorbic acid level in the plasma were run on seven persons receiving ascorbic acid and six persons receiving nicotinamide.

The specific daily therapy, started on April 9 and 21, 1941, consisted of 500 mg. of ascorbic acid in four tablets of 125 mg., each being given at an interval during the day. Further details in the administration of the therapy are contained in a previous paper (4). The daily dosages of nicotinamide and vitamin A for the control groups were 200 mg. and 100,000 I.U., respectively.

Among those receiving the ascorbic acid therapy, seven have since become unavailable through departure and could not be further followed. For similar reasons, two from the control group had to

[4] The ascorbic acid was generously furnished by Mead Johnson & Company, Evansville, Indiana.

withdraw. At regular intervals gum examinations have been conducted on the groups receiving the specific and control therapy, respectively. For the former, these examinations will form the basis for terminating therapy.

Description of Gingival Lesions

In the development and resolution of its specific lesions, avitaminosis C was found to be analogous in behavior to avitaminosis A (3), aniacinosis (4), and ariboflavinosis (1, 2, 8), though each is a distinct entity. This common pattern gave rise to a concept of deficiency states (9). In a deficiency disease the specific pathological process in a tissue has velocity, intensity, and sequence which determine its state. Categorized most simply according to these characteristics, it may be a mild acute, mild chronic, severe acute, or severe chronic process in a particular stage. Actually, once the chronic form sets in, it usually constitutes a base on which may be superimposed a mild or severe acute process.

According to the form, intensity, and stage of the pathological process, the condition of the gums in avitaminosis C was appraised. Both the acute and chronic processes were graded in three degrees, with each combination of form and intensity being divided into four successive stages. The predominant characteristics determined the stage, since manifestations of the previous and following phases were often present. Status was expressed in terms of both acute and chronic processes.

In many of the persons, the manifestations in the gums were seen readily in the gross; in some, certain characteristic features were detected definitely only by biomicroscopy. The series presented most of the states. It is understandable that the early stages in the acute and chronic processes were least frequent; for the first examination was in April and the persons were adults. By arranging the gingival lesions in a progressive series, according to their states, and by the reverse sequence of changes upon therapy, the course of the process in evolution and recession has been reconstructed.

In the gums the pathological changes appear in definite sequence. But since the characteristic changes of one stage do not disappear before evidences of the next appear, manifestations of the preceding and succeeding phase may be seen concurrently with the predominant signs of a given stage. Furthermore, different parts of the gum may show different stages. Although all sites are subjected to the same sequence of changes, they may not be affected synchronously. Rather, they are involved in a definite order: interdental papilla, the marginal, and then the alveolar gingiva. Both gums are not always equally affected; often but not invariably the upper gum shows the more advanced process.

It is convenient to describe the sequence of pathological changes in both the acute and chronic processes by following the arbitrary divisions of the rating scheme.

The acute process in the first stage presents the subsurface vascular papillae in an engorged and dilated state. Under the microscope these enlarged, congested capillaries are quite readily perceptible. In the mild degree this change is restricted largely to the interdental papillae and then the marginal gingiva. In a more intense condition the vascular reaction occurring more diffusely may be seen over the entire gum. There is little or no swelling.

In the second stage, the gum itself becomes red. In mild cases the heightened color is seen first at the points of the interdental papillae and then spreads to their bases and the marginal gingiva. It forms a serrated line across the free margin varying in intensity from light to vivid or dark red, but always deeper in shade than the less affected alveolar gum. In cases of more marked degree a pronounced redness extends uniformly over the entire gum. Very little or slight swelling is present at this time. The subsurface capillary papillae, beginning to show disturbance of their usual arrangement, become less discrete and distinct. The intense redness of the gums seems to be a diffuse coloration from engorged larger, deeper vessels. In the early part of this phase, however, many subsurface capillaries, much

congested, may appear as more intensely tinged points against a diffuse red background and impart to the gum a mottled appearance. The line of vascular demarcation usually present at the labial border of the gum, beneath which mucosal vessels disappear, may now be less distinguishable or entirely undistinguishable as the gingival surface assumes a near similar hue to the labial mucosa.

In the third stage, the reddened gum undergoes swelling. Here again, the intensity of the redness and swelling may be mild, moderate, or severe. In some instances these changes are restricted to the interdental papillae. More often the marginal gingivae, also affected, form a red, swollen collar projecting in high relief around the necks of the teeth. In such conditions the alveolar gingiva will be much less involved, usually showing more coloration than swelling. Very frequently the redness and swelling are present in the entire gum. The swelling may be so intense as to stretch the gum and give its surface a glossy, satiny finish. At the same time the tissue may be fiery red. Or when the swelling is disproportionately more marked than hyperemia, the emanation of redness from the underlying vessels may become so diffused by fluid as to give a pastel tint to the gum. The subsurface capillaries may not be seen.

At its free edge the gum may recede slightly, exposing more enamel surface of the tooth and increasing the length of the crown. If the gum is markedly swollen, its margin abutting against the tooth may form a trough. The gingival crevice may be enlarged and filled with calculus. Beginning formation of a pocket containing calculus and materia alba may be seen. Often the widened and deepened sulcus formed a well-developed pocket that was highly infected and filled with accumulated sordes and debris. At such a site the infection may be so destructive that the entire gum in that segment is broken down. From the resulting marked recession and thinness, a longitudinal groove appears in the gum. Infection of the gum is very common in this stage. Also most of the persons in this

series who had reported bleeding gums after brushing their teeth had changes typical of this stage.

More profound conditions seen in fully-developed scurvy, although not contained in the present series of cases, have been frequently described. The congested, spongy gums bleed readily, especially at their margin. In still more marked cases the enormously swollen gums are ulcerated and covered with a foul, necrotic material. Later the teeth become loose and may fall out; and the alveolar process undergoes necrosis. In such conditions, secondary infection with its added deleterious effects is especially conspicuous.

If the changes in the previous stage are not excessively severe or profoundly destructive, the acute process in its next stage shows beginning subsidence. At first the redness disappears with the swelling remaining. The gums appear greatly distended but pale in color. Probably infiltration takes place, either supplanting or masking the hyperemia and bringing about the disappearance of the redness. The interdental papillae and the marginal gingiva may be quite swollen and whitish in color, the distended tissue forming a collar around the tooth. In other instances the entire gum is greatly distended but exceedingly pale. In its pronounced form the tissue looks as though it were waterlogged. The subsurface capillaries are no longer visible.

In the chronic process the first stage is characterized by slight dilation and engorgement of the subsurface vascular papillae. The vascular reaction imparts a light redness to the gums. Shortly thereafter appears slight swelling. Coming first in the interdental papillae, the redness and swelling then extend to the gingival margin and finally, if of sufficient degree, over the entire gum.

In the next stage, the redness from the vascular reaction is gradually obscured by edema and probably by infiltration. At first seeming to contain excessive fluid and later to take on a more concentrated consistency and to be more opaque from a slight influx of light grey material, the gum is swollen but pale. The subsurface

capillaries are completely masked. The process may be confined to the interdental papillae and the margin adjacent to the teeth, or it may be present over the whole gum. It is probable that many of the acute processes subside into this stage and become chronic.

In the third stage, atrophy begins. The heavily infiltrated gum, which may show considerable distention and hypertrophy, now begins to manifest atrophy in the form of pitting. These pits are minute depressions. They appear first on the interdental papillae, then on the gingival margin adjacent to the tooth, and finally, may occur scattered over the entire gum. Although these pits, when large, can be discerned in the gross, they are best seen under the microscope. Indeed, only by this means can the beginning or smaller pits be observed. At first they are mostly subepithelial; they appear as funnel or cup-shaped depressions largely under the surface with the epithelium dipping only slightly at each point. Later, the epithelium is drawn in more deeply at each spot. In effect the surface seems to be studded with countersinks. Occasional isolated nodules may be seen. Along with these changes there is beginning retraction of the gum at its margin. In marked degrees of this stage the gum may be thick. Its general configuration then is rounded rather than modeled to the contour of the dental roots. In consistency, the gum is quite firm.

In the next stage, the atrophy becomes more profound. On the interdental papillae, the pits, which previously were so prominent, gradually disappear. The papillae show a decrease in size in all dimensions and gradually recede to the point of complete disappearance. The atrophic process may extend to the margin of the gum adjacent to the tooth. There may be extreme recession of the gum, leaving much of the cementum exposed. Consequently, the teeth show an increase in the length of their crowns and a loss of their root surface. Here again, pits that may have been present on the margin disappear, as the gum itself gradually recedes from its true position. In the most pronounced form, the entire gum is in-

volved. The interdental papillae have been lost, there is marked retraction around the neck of the tooth, and the remainder of the gum shows pronounced atrophy. Its color becomes white. In general, the contracted gums have a rounded contour. A few presented a rough nodular surface. Rotated, extruded, and loose teeth and diastema are very common. In this stage the line of vascular demarcation at the labial border of the gum is also undistinguishable.

It should be restated that in any state in the chronic process there may be an exacerbation. Consequently, an atrophic gum with receded interdental papillae, retracted margin, and pale color may become red and undergo distention, as an acute process is ignited. If the swelling associated with an acute process intervenes, in the stage of pitting, the gums may become so distended as to completely extinguish almost all of the pits.

For both the acute and chronic processes, whether in the interdental papillae, gingival margin, or the entire gum, the changes were in general quite uniform from segment to segment in the field of observation in any one gum, though they were often accentuated by infection in one or two localized sites. Very frequently one gum was more severely affected than the other. It should be emphasized that both the acute and chronic gingival changes were noted in two edentulous adults.

None of the persons showed any skin lesion.

Values for Ascorbic Acid in Plasma

From the group of forty-nine persons, blood samples for the determination of ascorbic acid concentration in the plasma were obtained from forty-two prior to therapy. It was found that 43 per cent of the latter had concentrations below 0.6 mg., the level frequently adopted as a significant dividing line; while 21 per cent had concentrations below 0.2 mg. per 100 ml. According to the usual interpretation of blood levels, 43 per cent of the persons might be suspected to have avitaminosis C. In contrast, it is to be remem-

Gingival Ratings	Concentration of Ascorbic Acid in Mg. Per 100 Ml. Plasma							
	0.00–0.19	0.20–0.39	0.40–0.59	0.60–0.79	0.80–0.99	1.00–1.19	1.20–1.39	1.4 +
III Sl One							1	
III Sl Both					1		1	
III Mod One	3	2	1	4	2			1
III Mod Both	1	2	1	1		2		
III Mkd One	2					2		
III Mkd Both	3		2	2		2	1	
IV Sl Both		1			1			
IV Mod One				1	1			
IV Mod Both								1
Total	9	5	4	8	5	6	3	2

Table 1. Values for concentration of ascorbic acid in plasma are arranged according to the corresponding ratings of the gums for their acute process.

bered that all had gum lesions; therefore, judged by tissue criteria, 100 per cent had avitaminosis C. It is interesting that 26 per cent, all with gingival lesions, had ascorbic acid levels of 1 mg. per cent or more.

When the values for the concentration of ascorbic acid are matched against the ratings from tissue changes in the acute process, it is seen that most of the values are on persons with lesions at the peak of an acute condition; and that of these persons with gingivae in this stage just as many had high as had low values for ascorbic acid (Table 1). When the values for ascorbic acid in the plasma are compared with the ratings for chronic gingival lesions, it is found that there is no evident relationship. In most stages and degrees the values are distributed just as frequently among the high as among the low levels (Table 2).

Results from Capillary Resistance Test

The capillary resistance test conducted on sixteen persons prior to therapy gave results which showed no relation to either the values for ascorbic acid concentration in the plasma or the status of the gums.

Changes on Therapy

At the outset it should be stressed that no scaling was done. In-

Gingival Ratings	Concentration of Ascorbic Acid in Mg. Per 100 Ml. Plasma							
	0.00–0.19	0.20–0.39	0.40–0.59	0.60–0.79	0.80–0.99	1.00–1.19	1.20–1.39	1.4 +
III Sl Both							1	
III Mod Both				1	1			1
III Mkd One			1	3	2	2		
III Mkd Both	2	4	1	3	2	3		1
IV Sl One								
IV Sl Both			1					
IV Mod One	2	1		1		1	1	
IV Mod Both	1		1					
IV Mkd One	1	1	1				1	
IV Mkd Both				1				
Total	6	6	5	9	5	6	3	2

Table 2. Values for concentration of ascorbic acid in plasma are arranged according to the corresponding ratings of the gums for their chronic process.

deed, no mechanical measures were applied to the gums and teeth other than whatever brushing the persons may have been accustomed to give them. For many persons brushing was probably somewhat infrequent; nor were they advised to be regular in it.

With most of the gums showing an acute imposed on a chronic process, the first response to ascorbic acid therapy was improvement and removal of the acute condition.

In the late stages of the acute process with infiltration and hypertrophy, either all the interdental papillae and collar or the entire gum lost much of its infiltration and swelling through therapy. Also, the usual pattern of the larger vessels was reestablished. Vascularity became quite pronounced in the labial mucous membrane and where it disappeared under the gum it formed a line of demarcation. In what was the most swollen part, namely, the interdental papillae and the collar, the tissue assumed a reddish hue, due to both removal of the infiltration and the reestablishment of vascularity. In many instances the color was heightened still more around the collar for a time when secondary infection had not yet been dispelled from very large crevices. Often this infection had been seemingly quiescent in this stage but became aroused with

reestablishment of the circulation. Thus, in a waterlogged tissue with slight redness in the interdental papillae and collar and rather pronounced crevices with a secondary infection, the removal of the swelling may at first increase the intensity of redness in the infected interdental papillae and collar, while the remainder of the gum will be freed of the acute process. Ultimately, if no devitalized teeth or foreign bodies are present, the infection is expelled and the acute process disappears.

In the stage characterized by hyperemia and swelling, there was diminution and removal of both manifestations. What in severe degree had been a red swollen gum became much thinner and paler. Here again, the vascular supply in the mucous membrane leading to the gum leaves a line of demarcation where it passes under the gum. Often, where originally there was intense swelling everywhere, but particularly in the interdental papillae and collar due to pronounced crevices with marked secondary infection, swelling was for a time only slightly diminished in the latter sites but almost entirely removed from the remainder of the gum. Here the secondary infection temporarily delayed the disappearance of the acute process. Where the crevice was not excessively large and the surrounding collar showed moderate swelling, there was a diminution in retraction and a disappearance of the swelling at the margin.

In mild degrees in this stage, where redness and swelling was largely restricted to the interdental papillae and collar, these manifestations disappeared. When they were present over the entire gum, but were slightly more intense in the interdental papillae and collar because crevices with secondary infection were present, therapy at first removed the redness and swelling from the alveolar gingiva. Absolutely, much of the redness and swelling from the interdental papillae and collar were also removed; but in the presence of secondary infection, enough of the manifestations remained for a time so that the margin stood out in contrast to the remainder of the gum which had already been restored to its natural color and

thickness. Some time thereafter, the redness and the swelling disappeared from the interdental papillae and collar.

It is worth while to emphasize the conditions which retard the resolution of the acute process. These conditions occurred mostly in the stages just discussed, namely, those characterized by swelling and redness or infiltration. For one thing, in this series a secondary infection, almost always focal in disposition, was frequently associated with the acute deficiency process in its climactic stages and aggravated the gingival condition at its site. This infection had to be expelled before the acute deficiency process would disappear and normal gum tissue at that point show complete restoration. Under this circumstance disappearance of the acute deficiency process from there during ascorbic acid therapy was slowed. Where no devitalized tooth was present, the secondary infection localized and drained spontaneously in response to ascorbic acid therapy. When the infection was severe, it has taken a year in some instances to resolve it and extinguish the acute avitaminotic process. With no therapeutic measure other than ascorbic acid, the signs of localized infection and the acute process vanished. Another circumstance, a devitalized tooth in whole or fragment, located in the site of the secondary infection, was apt to slow the therapeutic response. When a devitalized tooth was present in the focus of infection, it was often found advisable to have it extracted. Thereafter, the acute process rapidly disappeared. The devitalized tooth perpetuated and prolonged the infection. Whether such a tooth acting as a foreign body was sometimes *per se* the retardant, or whether it furnished a nidus for infection which was always the retarding factor, cannot be said. Practically either situation is incompatible with healthy gingival tissue.

In the stage characterized mainly by redness, therapy reestablished vascularity, with its characteristic line of demarcation, and at the same time removed redness from the gums, leaving them in their natural color.

Since the acute process in many instances may mask much of the chronic changes, removal of the former then brings out the latter underlying condition with its full manifestations. Very often a gum swollen and showing only traces of pitting here and there, is seen to be heavily pitted upon dissipation of the swelling. Similarly, interdental papillae may, prior to therapy, be apparently normal in size and position, but upon removal of the acute process with its swelling, they may be left in their actual basic condition, atrophic and contracted.

After the acute changes are expelled, the chronic process undergoes recession.

In the advanced chronic stage characterized by atrophy of the entire gum, including the interdental papillae, with marked retraction, the response to therapy occurred first in the alveolar gingiva where a new material was laid down, giving increased thickness to the gum and imparting to it a whiter color. Teeth that were previously loose became firm. Where much of the infection had disappeared from the margin, the crevice became much smaller and the gum tended to move to its accustomed place, obliterating much of the crevice.

Persons with gums of marked degree in this stage usually also had an acute process and one or more heavily infected areas. Consequently, in these instances the acute deficiency and the infective processes have taken most of the year to disappear and the chronic process has just begun to undergo recession. But the changes on therapy in the less intensely involved gums in this stage give an indication of the course of events.

In moderate and slight degrees of this stage, after the acute process has withdrawn, the deposition of a new substance throughout the gum may be observed. Although this material was laid down over the entire gum, it seemed to appear first on the margin and interdental papillae sites which were most seriously affected. At this time also, not only may the crevices begin to be obliterated, but the

interdental papillae which were partially contracted may show extension to more nearly their normal length. With the deposition of a new substance throughout the gum, any pitting disappears.

Gingival tissue in an advanced chronic stage with little acute process is much less vascular than in the normal condition. Its heavy infection may be low grade. Then the first response to therapy is restoration of the vascularity. From this response, together with the reaction to the infection, the gum may temporarily take on pronounced redness. As the infection is overcome the gingival tissue then gradually assumes its natural, normal color which initially it had lacked.

In the cases of marked degree in the stage characterized principally by generalized pitting, there was laying down of material throughout the gum. Frequently this deposition was seen first in the depths of the pits, its whiteness giving the gums under the microscope a dappled appearance. With this material filling in the gum, the pitting on the surface then tended to disappear. Usually, it disappeared first from the alveolar area so that at one stage in the recovery period a gum that had previously been entirely pitted now showed pitting only in the interdental papillae. At this time, the interdental papillae also began to resume their normal height. Along with the extension of the papillae came the climbing of the collar to cover the tooth and the disappearance of the crevice. Also, the subsurface capillaries began to reappear in orderly arrangement, at first emerging only slightly but later to their usual position. In lesser degrees with the pitting limited to the interdental papillae and margin, the course in recession has been similar.

The gum in the stage marked by distention and infiltration lost its swelling. If in this change, pitting or slight atrophy of the interdental papillae was unmasked, the laying down of new material filled in the area and gave it more substance. The papillae and margin began to regain their usual positions, while the entire gingiva through deposition of new material added substance.

Control groups receiving nicotinamide or vitamin A have shown no improvement in their gums.

Two months after therapy had been started, determinations for the concentration of ascorbic acid in plasma were conducted on seven persons receiving ascorbic acid, five of whom had had initial values below 0.60 mg. per cent. After two months on this therapy, all seven persons had values higher than 1.25 mg. per cent, one as high as 1.76 mg. Yet, at this time, their gingival tissue had not appreciably changed in response to the therapy.

Of six control persons receiving nicotinamide who had initial values for ascorbic acid below 0.60 mg. per cent, only one had a concentration above that level two months later with their usual diet as their sole source of ascorbic acid.

Discussion

Since scurvy arises from a deficiency or disturbance in ascorbic acid, it is pertinent to consider the recorded manifestations of that disease, especially changes in the gums. In the long recorded history of scurvy, many reports are on epidemics occurring among armies, naval- and merchant-vessel crews, and civilians of besieged cities.

In his celebrated treatise on scurvy, Lind reviewed critically all the previous writings on the subject (10). He says: "The first description of a true scurvy [in armies] that I have met with, is what occurred in the Christian army in Ægypt, about the year 1260, under Lewis IX. But there mention is made, not only of the legs being affected, but also of the spots. The fungous and putrid gums are particularly described."

From the records of an outbreak on Jacques Cartier's second voyage to Newfoundland in 1535, Lind quotes (11): "... some did lose all their strength, and could not stand upon their feet; then did their legs swell, their sinews shrunk, and became as black as a coal. Others had also their skin spotted with spots of blood, of a purple colour. It ascended up to their ancles, knees, thighs, shoulders, arms

and neck. Their mouth became stinking; their gums so rotten, that all the flesh came away, even to the roots of their teeth; which last did also almost all fall out." In subsequent accounts of the disease these signs are invariably mentioned, as well as less constant manifestations, although various observers placed them in different sequences.

Echthius in 1541 arranged the symptoms into two classes (12). The first, which appear at the beginning, comprise lassitude; weakness of the legs; itching, redness, and pain of the gums; and darkening of the complexion. He observes that where all these symptoms concur, an approaching scurvy may be foretold. Under the second class he enumerated the succeeding and more certain signs: a fetid breath; a spongy swelling of the gums, which are apt to bleed, with loosening of the teeth; eruption of spots on the legs.

Wierus in 1567 wrote that weakness and pain in the legs was felt at the approach of the disease; the flesh of the gums was often destroyed to the roots of the teeth; small hemorrhagic spots appeared on the legs (13). Similarly, Brunerus (14) stated that violent pains in the legs preceded the scurvy, and that the spots and putrefaction of the gums followed soon after. But Dodonaeus (15), reporting in 1581 on an epidemic of scurvy, stated that many persons did not manifest the spots, rather their gums were chiefly affected. Also, Eugalenus in 1604 listed putrid gums as the first sign and hemorrhagic spots as the next manifestation (16).

Dividing the course of scurvy into three stages, Lind himself (10) described the symptoms in the order of their appearance. As characteristic of the first stage he mentioned: change in complexion, lassitude, stiffness and weakness of knees, gum changes, hemorrhagic spots on the skin, and beginning edema in the legs. "Their gums," he reports, "... swell, and are apt to bleed upon the gentlest friction. Their breath is then offensive; and upon looking into their mouth, the gums have an unusual livid appearance, are soft and spongy, and become afterwards extremely putrid and fungous, one of the

most distinguishing signs of the disease." He asserts: "These are the most constant and essential symptoms of the malady in the progress of its first stage. But a diversity is sometimes observed in the order of their appearance." In the succeeding stages, the condition of the gums grew worse.

Early in the disease, Himmelstiern noted (17), the gums were pale and less turgescent than in their healthy condition; later in the spring and summer months they showed livid, soft swelling, to the point of thick puffiness. Then pain, swelling, and spots appeared in the knees. Arranging the signs of scurvy into four classes or stages, Curran cited gingival changes in all classes (18). Of the gums in the first class, he stated that they were never natural. He described pale, thin, as well as red, swollen gums. He wrote: "A diseased condition of the alveolar margin of the gums seems to be the most constant of the characteristics of scurvy." Krebel, dividing the disease into three stages or degrees, likewise mentioned pale, thin or red, swollen gums (19). Other clinicians in the same era regarded gum affections, edema in the legs, and hemorrhagic spots as a basis of diagnosing scurvy (20-23). Immerman stated that after an initial or prodromal period, the scorbutic condition appeared in the majority of cases, but not always, in the gums (23). Gingival lesions are regarded as remarkably constant by some present-day observers (24, 5, 25).

Besides the main characteristics of scurvy in adults, just presented, the disease as it occurs in infants has been especially studied. In 1878 for the first time, Cheadle (26), reporting on the concurrence of swollen or bleeding gums and swollen tender thighs in three infants, characterized the condition as scurvy. Barlow, in 1883, reviewing the literature on twenty previous cases and presenting observations on eleven new cases, demonstrated that the involvement of the thighs was subperiosteal hemorrhage (27). In fifteen cases there were changes in the gums; in six, none; in the remaining ten, the gums were not mentioned. Barlow believed that the absence

of sponginess in the latter instances was the reason his colleagues had dismissed scurvy as a possible diagnosis, an interesting indication of the diagnostic emphasis placed on gingival changes at that time. For the condition he proposed the name infantile scurvy, "which is distinguished from adult scurvy by the greater incidence of the disease of the bone." It was found to be most prevalent between the ages of nine and eighteen months.

In 1894 Barlow (28), advancing an explanation of this seeming variance between gums and subperiosteal manifestations in infantile and adult scurvy, laid more stress on the gingival changes. He wrote: "The condition of the gums is very important. Defective observation on this point has led to frequent misconceptions as to the nature of the disease. Stated generally, the gum condition may be said to bear a definite relation to the number of teeth which have appeared. If several teeth have appeared, considerable sponginess of the gums may be manifest. Fleshy swellings form, which even project from the mouth and give rise to bleeding and foeter. But if only a few teeth have appeared the sponginess may be slight though definite, forming a narrow, fleshy ridge round each tooth. If no teeth have appeared the gums may be normal or may present small, bluish extravasations over the sites of the on-coming teeth."

Continuing, he stated: ". . . with respect to the gums, we may classify the infantile cases into those which have limb symptoms with spongy gums, and those which have limb symptoms without spongy gums, and we have found that the state of spongy gums is practically conditioned by the presence of teeth. If there are several teeth the sponginess is efflorescent, and in the severe cases the foeter, the bleeding, and the protruding tumours are indistinguishable from what we find in typical scurvy. If there are no teeth there is no sponginess, though there may be found on careful inspection minute ecchymoses. Now the greatest stress has been laid upon the gum condition in adult scurvy; but there is abundant evidence that a toothless man may present the limb weakness, the cachexia, and

anemia, and yet show no sponginess of gum whatever. In mild cases of land scurvy also it is constantly observed that the sponginess is limited strictly to the neighbourhood of those teeth which remain; and if there be large intervals where the teeth have been lost no sponginess appears in those intervals. I may here refer to a series of five cases which have been under my observation at different periods, but which in age were beyond the limit of infancy. In these five cases—children from two to ten years of age—there was undoubted scurvy, produced, I believe, by a curious hysterical antipathy to vegetables and meat. The gum affection was generally more severe than that of the infantile cases above described. The limb affection resembled that of the infant cases, but was less severe. The study of these cases occurring in childhood shows, I believe, a middle term (so far as the symptoms are concerned) between the infantile group and adult scurvy."

Subsequent investigators have, in the main, subscribed to this view (29-34). But Netter (35) and Bardin (36) have particularly stressed changes in the gum, in addition to the swelling in the leg. Epstein (37) has declared: "... in the edentulous jaw the gingivitis is usually not absent. It is only less distinct and makes itself manifest in a slight reddening, swelling and edematous condition of the gum over the alveoli of the upper incisors. As a rule the gingivitis is detectible simultaneously with the bone swelling, exceptionally it first appears later." In a like vein Holt and McIntosh (34) assert: "Changes in the gums are commonly found in the early stage, although they are rarely the first symptom to attract attention."

Characteristic changes of scurvy in the bone during infancy as well as later during the period of growth have been studied in human beings (38, 39) and experimental animals (40-43). Both macroscopic and microscopic observations have been made. Moreover, the scorbutic manifestations perceptible in roentgenograms of the skeleton have been described (44, 45).

Many clinicians have attempted to describe the sequence of mani-

festations in scurvy; several have tried to divide the course of the disease into stages (10, 18, 19, 46). Most of the investigators, interested in early diagnosis, set down their observations on the earliest sign of scurvy. Moreover, they distinguished a period before the disease proper appeared, before its well-known signs could be recognized. Others later conceived that scurvy might exist below the level of clinical detection for a prolonged duration. Despite the variety of names by which these states were designated—premonitory signs, prodromal period, forme fruste, prescurvy, abortive scurvy, latent state—despite the differences in concepts about the states and their points of identification, all agreed that most of the scurvy occurred in these states (10, 12, 13, 14, 18, 23, 41, 47-57).

Still later with the recognition that scurvy appeared in still another state, the so-called monosymptomatic state, the aim was to elicit or detect that sign by appropriate methodology before it became grossly perceptible. As was generally agreed, the three principal manifestations of scurvy were: hemorrhages on the skin, bone changes, and gum lesions. Methods for detecting the first two manifestations in their early or mild state have already been widely applied. Detection of the third, gingival changes, forms the content of the present paper.

Latent fragility of the capillary walls, a state predisposing to hemorrhage, has been tested by determining whether petechiae or ecchymosis could be produced on a skin site by application of measured pressure. Originally, capillary fragility was described in association with a variety of pathological states (58-62). In 1914 Hess described tests with positive pressure showing impaired capillary resistance in scorbutic infants (63). Using the same procedure and counting petechiae, Göthlin suggested that it be used as a measure of vitamin C status (64). Meanwhile, a method applying negative pressure had been developed (65) and applied to detection of avitaminosis C (66).

The limitations of this procedure have been fully discussed (67,

68). Besides yielding a high degree of variation in values, it has proved disappointing in the most important respect, the detection of early or mild avitaminosis C. In the present work, as in numerous instances, the results from the method were entirely inconclusive.

In an excellent paper on the recognition of scurvy, Park and coworkers have described the early changes in bone as seen in the roentgenogram (69). In the practice of pediatrics this means of revealing early scorbutic changes has been extremely valuable. As a procedure for detecting avitaminosis C in the general population, however, it has certain limitations. It is applicable to a narrow age period, infancy and childhood. Indeed, it has never been asserted that detection of bone changes by x-ray, in its present application, would be sufficiently sensitive to allow appraisal of vitamin C status.

In considering gum lesions as a basis for detecting avitaminosis C, it is essential to recognize that they present manifestations other than hemorrhage. In fact, when hemorrhage occurs the pathological process in the gum is far advanced; for bleeding is preceded by a sequence of definite changes. Furthermore, hemorrhage is a contingent phenomenon; the expression "apt or tend to bleed" appears repeatedly in the literature. Therefore, if hemorrhage was the only criterion, if earlier changes were ignored, the full value of observations on the gums in detecting incipient and low-grade states would be impaired; with its range of application and sensitivity thereby greatly restricted, the true usefulness of the procedure in appraising vitamin C status would be misjudged. A minority of observers based their diagnosis solely on hemorrhage, and apparently accepted anything prior to that as insignificant or normal. However, most, as will have been noted, distinguished a course of changes in the gums. Indeed, some rightly designated these manifestations as gingivitis (31, 35, 37, 39).

More recent evidence points even more specifically to gum changes as an integral part of avitaminosis C. In addition to the epidemics of scurvy with gingival manifestations already cited, nu-

merous outbreaks occurred during World War I. Reports on them described gingivitis in various stages. The changes in the gum were characterized as early (46, 70), constant (71), and very marked (37, 72-76). By a few observers they were represented as prominent but absent in some cases (77-80); by one, as early or late and often absent (81).

It is interesting that as early as 1878 Cheadle with long-range vision anticipated that scurvy with only gingival lesions might occur (26). He wrote: "I have said that cases of scurvy are rare amongst children in large towns, and instances of the fully-developed disease undoubtedly are so. It seems to me possible, however, that the cases of ulcerative stomatitis, which are not infrequent amongst ill-nourished, neglected children, may be due to the scorbutic condition—i.e., imperfectly-developed scurvy. The foul ulceration of the gums closely resembles the condition of these parts presented by cases of scurvy where the swelling of the severest stage has subsided, and the general cachectic condition is analogous to that which exists in scorbutic disease."

In 1941 Crane and Woods (82) reported an outbreak of avitaminosis C, among a group of children, characterized clinically by gingival changes. Similarly, in a dental clinic, a group of outpatients affected only with periodontal disease were found to have avitaminosis C (83).

Prominent among the signs of scurvy produced experimentally in animals by a vitamin C-deficient diet were typical gum changes (40, 84, 85). Furthermore, periodontal disease comprising alveolar atrophy was diagnosed histopathologically in animals with restricted intake of vitamin C (86-88). Most convincing of all, numerous reports asserted that gingivitis, in many instances far advanced, severe and complicated by secondary infection, was cured in persons by administration of vitamin C. In the first studies lime juice (77), lemon juice (54), and orange juice (89) were used; in later investigations, pure ascorbic acid (82, 90-97).

These various lines of evidence support the thesis that gum lesions are specific and invariable manifestations of avitaminosis C. It is evident that reports on the occurrence of gingival changes depend on the examiners' concept and criteria. Furthermore, because of these differences in diagnostic standards and because many observations were on fully-developed scurvy, with its several manifestations already present, it is not possible to conclude from the literature on scurvy in persons which sign was first in appearance. Evidence from experimental animals, if applicable, indicates that tooth pulp is the site of initial change (41, 98). Zilva and Wells stated (98): "Our animal experiments show definitely that the scurvy may be of an extremely mild form, and yet produce very marked changes in the teeth." Practically, however, the present work shows that the gums are affected sufficiently early to serve as a useful manifestation.

In all respects, therefore, examination of the gums forms a satisfactory basis for appraisal of vitamin C status. The gingival tissue is readily accessible to observation. Its changes are specific and constant in occurrence. They are present in all states of avitaminosis C: they appear early, persist and reflect its course. From them any state may be rated in terms of form, stage, and degree. The biomicroscope is exceedingly sensitive in revealing the very early and slight tissue changes. Low-grade states, whether prolonged or not, may be detected by it. The slighter the change and the closer it approaches perfection, the more the biomicroscope is required.

With the development of accurate methods for determining the concentration of ascorbic acid in blood and urine, analyses were conducted on these fluids, after a fasting period or a test dose, as a means of appraising vitamin C status. There has been a strong trend towards general acceptance of the results from these procedures as the true index of bodily status with respect to vitamin C. Indeed, the reliability of other methods of appraisal has been gauged by comparison with blood values as the criterion. Yet Greenberg,

Rinehart, and Phatak cautioned (99): " . . . the estimation of the reduced plasma ascorbic acid is only a measure of the immediate nutritive or metabolic level relative to vitamin C, and is dependent on recent dietary habits to a large degree. Although it is an index of the vitamin C nutrition at the time of the test, in a single case a low level does not imply tissue injury or scurvy (either clinical or subclinical). The latter results from the operation of suboptimal or low metabolic levels over some period of time. Conversely, a good or high level would not indicate that deficiency had not operated to produce tissue injury in the past."

In line with this statement, Crane and Woods, studying an acute outbreak of scurvy in children by comparing gingival condition with ascorbic acid concentration in plasma, both in the autumn and the following spring, found that seven of seventeen children with consistently high ascorbic acid values on both occasions had gingival inflammation at one or the other examination; while fourteen of twenty-five children with inflammation of at least six months' duration had high values on one or the other occasion. Similar data in the present paper from comparison of ascorbic acid values with the states of the gingival lesions—with a more sensitive method of detecting and more rigid criteria of rating pathology in the gums—reveal an even less constant relationship. These results, far from demonstrating that the blood level is a trustworthy criterion for comparison of other methods, show that it has very marked restrictions as a method for appraising vitamin C status.

The reasons why blood values may not show a very close relationship to the tissue rating have already been explained (9). The following points are mainly responsible: the blood value may change seasonally as well as fluctuate very frequently, responding quickly to change in intake of ascorbic acid; the concentration of ascorbic acid in the blood changes sooner and much more rapidly than the tissue state, both in the evolution and recession of the deficiency disease; avitaminosis C is widely prevalent in the tissues in

the chronic state; improvement in the diet may raise the blood values with very little effect on the status of the chronic tissue lesion.

If the tissue is normal a low blood value is significant. In the initial attack, the lowered concentration of ascorbic acid in the blood would be the first demonstrable change and would be followed shortly thereafter by tissue change. But with widespread prevalence of avitaminosis C, particularly in the chronic form, and its establishment early in life in most persons, a normal state in the gingival tissue is relatively infrequent. Hence, the blood method as a primary screen for the appraisal of vitamin C status has in reality a very limited range of application. Furthermore, when chronic changes are present—and this is the common eventuality—they recede very little upon any sustained improvement in diet and only very slowly under persistent therapy, while the ascorbic acid concentration rises immediately in response to either event. Temporarily or consistently, therefore, the blood value may be moderate or high without demonstrable recession in the existing lesion. Appraisal from the blood value alone would be entirely misleading.

From the concept of deficiency states (9) it may be seen that avitaminosis C includes all forms, degrees, and stages. Scurvy represents the severe acute state. It is interesting that several investigators have mentioned one or another of the various other states embraced by this concept. Hess (49) recognized three types of scurvy: the florid, with well-developed signs of the full-blown condition; the subacute, the commoner form, presenting a group of incompletely developed symptoms; the latent, resulting from a negative balance in ascorbic acid during the period prior to the onset of clinical manifestations. According to his conception of the course of events, the latent "may advance no further, . . . it may gradually merge into subacute scurvy and develop no further," or "the typical gradation may ensue, of latent, subacute and florid infantile scurvy." Several investigators have graded avitaminosis C into three degrees: one rated scurvy, using changes in the gums as a

principal part of the basis (72); the others distinguished degrees of gingivitis (89, 82).

In scurvy produced in animals, Tozer differentiated the chronic from the acute form on a time basis (100). She stated that the chronic form varies in severity according to the degree of deprivation of vitamin C. Using a different terminology to express intensity, she described mild and severe degrees for both the acute and chronic forms. Recognizing these various states, Höjer (41) employed still another nomenclature. Ferrario (101, 102) also produced acute and chronic scurvy in guinea pigs. Clinically periodontal disease is classified into gingivitis and alveolar atrophy, according to Boyle (86-88). He pointed out that gingivitis and marked alveolar rarefaction occur in acute scurvy. Upon producing chronic avitaminosis C, he noted that similar changes took place at a slower rate, particularly was diffuse alveolar atrophy a conspicuous feature.

It will be noted that in the present work many of the persons showing most marked atrophic changes in the gingiva manifested signs of alveolar atrophy. Indeed, the changes observed in the acute and chronic states, respectively, include the two aspects of periodontal disease. Earlier investigators observed pale, thin gums without distinguishing them as chronic gingival changes. Most of the literature on avitaminosis C, however, pertains only to the severe acute form. Generally the mild acute, mild and severe chronic states, the most common states of avitaminosis C among the population, have not been recognized, differentiated, and appreciated.

Considerable evidence shows that there is a high prevalence of avitaminosis C (103), including much of rather severe degree. Few persons have throughout life faithfully observed a dietary regimen satisfactory in its vitamin C content, or escaped the many other causes contributing to the deficiency state. Of the many with tissue affected, few have taken measures to restore it completely. In the gums are registered the cumulative changes, an arrested, incompletely receded, or progressive chronic as well as a fresh acute

process. Furthermore, the standard of perfection in the tissue is highly exacting and biomicroscopic detection is very sensitive. All these points make the high prevalence of avitaminosis C understandable.

Various criteria of recovery have been reported in the treatment of avitaminosis C with ascorbic acid. In some studies on gingivitis, therapy was terminated when the gums no longer bled on application of pressure. In treatment of scurvy, therapy was discontinued when the body was presumably saturated with ascorbic acid, as judged by analyses on blood and urine. But saturation does not mean restoration of tissue. It has been seen in the present work that all the blood values on the persons receiving ascorbic acid became very high in two months while the gums had as yet shown only slight improvement. If recovery is judged by hemorrhagic or saturation criteria, the patient would be discharged incompletely treated. Furthermore, there is much chronic avitaminosis C, some with secondary infection, and a long period is required for recession. It should be observed that in treating gingivitis with ascorbic acid for only a short period, even several months, and noting little or no apparent improvement in some instances, investigators may be misled in their conclusions on the effectiveness of the therapy, because they are dealing with a chronic condition, perhaps also secondarily infected, for which a long period of therapy is necessary. All these points suggest that, in the past, avitaminosis C has not been completely treated. To be complete the therapy should be continued until the gums show no abnormality.

It should be mentioned that the prevalence of secondary infection noted in the present work among some of the persons with advanced or severe gingival conditions parallels previously reported occurrences in association with gum lesions in avitaminosis C (24, 33, 39, 78).

Summary

Of forty-nine persons in a low-income group, all had gross or

microscopic gingival lesions characteristic of avitaminosis C.

Following administration of ascorbic acid to twenty-five persons in this group, the gingival lesions in two have now almost entirely receded, as judged in all instances by biomicroscopic examination. The initially more severe lesions in the others of the therapeutic group have receded markedly, some nearly completely.

In all cases the striking feature is the very long period of time required for complete recovery, more than a year even with therapy of high potency. In this respect, avitaminosis C is similar to avitaminosis A, ariboflavinosis, and aniacinosis. This common feature, the slow response, leads to a concept of the deficiency states in which the importance of chronicity, as well as mild states, is emphasized.

Those persons receiving vitamin A or nicotinamide have shown no improvement in the gums.

For detection of avitaminosis C, examination of the anterior gums is recommended as a simple, convenient, objective method. When biomicroscopic is combined with gross examination, all forms, degrees, and stages of avitaminosis C may be noted and graded.

The marked prevalence of avitaminosis C is explained.

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